Open access • Journal Article • DOI:10.30875/4180E4E0-EN

Product patents and access to innovative medicines in a post-trips-era

Jayashree Watal, Rong Dai

Institutions: Georgetown University Law Center, Graduate Institute of International and Development Studies

Published on: 17 Jul 2019 - Social Science Research Network (Geneva: World Trade Organization (WTO))

Topics: TRIPS architecture

Watal, Jayashree; Dai, Rong

Working Paper

Product patents and access to innovative medicines in a post-trips-era

WTO Staff Working Paper, No. ERSD-2019-05

Provided in Cooperation with:
World Trade Organization (WTO), Economic Research and Statistics Division, Geneva

Suggested Citation: Watal, Jayashree; Dai, Rong (2019) : Product patents and access to innovative medicines in a post-trips-era, WTO Staff Working Paper, No. ERSD-2019-05, World Trade Organization (WTO), Geneva, https://doi.org/10.30875/4180e4e0-en

This Version is available at:
http://hdl.handle.net/10419/195778

Staff Working Paper ERSD-2019-05 **4 April 2019**

World Trade Organization

Economic Research and Statistics Division

PRODUCT PATENTS AND ACCESS TO INNOVATIVE MEDICINES IN A POST-TRIPS-ERA

Jayashree Watal and Rong Dai[1]

Manuscript date: 28 March 2019

[1] Watal: Counsellor, WTO. Dai: intern, WTO; PhD candidate, the Graduate Institute.

We gratefully acknowledge the contribution of Peter Stephens, Director, Healthcare Stakeholders, IQVIA for not only providing the data but for explaining all its nuances to us. We also acknowledge useful comments/edits contributed by those who read earlier drafts, notably Jean-Louis Arcand, Margaret Kyle, Yi Qian, Rahul Mukherjee, Julio Raffo, and Antony Taubman.

PRODUCT PATENTS AND ACCESS TO INNOVATIVE MEDICINES IN A POST-TRIPS ERA

JAYASHREE WATAL AND RONG DAI[1]

Manuscript date: 28 March 2019

Abstract

This WTO working paper studies availability and affordability of new and innovative pharmaceuticals in a post-TRIPS era. The WTO's TRIPS Agreement (TRIPS) makes it obligatory for WTO members – except least-developed country members (LDCs) - to provide pharmaceutical product patents with a 20-year protection term. Developing country members, other than LDCs, were meant to be compliant with this provision of TRIPS by 2005. This study investigates two questions in this context: (1) How does the introduction of product patents in pharmaceuticals affect the likelihood of pharmaceutical firms to launch new and innovative medicines in those markets? (2) For launched new and innovative medicines, how much do patent owners or generic pharmaceutical firms adjust their prices to local income levels?

Using launch data from 1980 to 2017 covering 70 markets, the study finds that introduction of product patent for pharmaceuticals in the patent law has a positive effect on launch likelihood, especially for innovative pharmaceuticals. However, this effect is quite limited in low-income markets. Also, innovative pharmaceuticals are launched sooner than non-innovative ones, irrespective of the patent regime in the local market.

Using a panel data set of originator and generic prices from 2007 to 2017, the study finds evidence of differential pricing for both originator and generic products. Overall, originators differentiate by about 11% and generics by about 26%. Differential pricing is larger for pharmaceuticals to treat infectious diseases, particularly for HIV/AIDs medicines, than for non-communicable diseases. However, pharmaceutical prices are far from being fully adjusted to local income levels in either case. However, competition, especially that within a particular medicine market, can effectively drive down prices in both originator and generic markets.

Key words: intellectual property rights; patents; TRIPS; pharmaceuticals; pharmaceutical prices; differential pricing; developing countries;

JEL codes: O34; I11; I19; F19.

[1] Watal: Counsellor, WTO. Dai: intern, WTO; PhD candidate, the Graduate Institute.

We gratefully acknowledge the contribution of Peter Stephens, Director, Healthcare Stakeholders, IQVIA for not only providing the data but for explaining all its nuances to us. We also acknowledge useful comments/edits contributed by those who read earlier drafts, notably Jean-Louis Arcand, Margaret Kyle, Yi Qian, Rahul Mukherjee, Julio Raffo, and Antony Taubman.

1 INTRODUCTION

Access to new, innovative medicines[2] can be analysed from two perspectives: availability of these new products on the domestic market and the affordability of these products in each market. The patent regime is especially important for pharmaceutical firms to make launch and pricing decisions, which further affects access to medicines in the local market. The WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) makes it obligatory for WTO Members – except least-developed country members (LDCs) - to provide pharmaceutical product patents with a 20-year protection term. Developing country members other than LDCs were meant to be compliant with this provision of TRIPS at the latest by 2005. LDCs have currently up to 2033 to do so. In this context, two precise research questions are posed:

i. What is the effect of the implementation of TRIPS in domestic law, and more precisely, the availability of product patents for pharmaceuticals, on the launch of new and innovative pharmaceuticals in different markets?

ii. Once launched, how much do originator and generic firms take affordability into account in pricing these new products in different markets?

We investigate these two questions using pharmaceutical data from IQVIA[3] for 578 molecules in up to 70 markets. To examine the effect of the introduction of product patents on launch likelihood of new medicines, we use launch data from 1980 to 2017. In the price study, we analyse pricing strategies of pharmaceuticals with panel data from 2007 to 2017. Our paper contributes to the literature from the following perspectives. First, we differentiate between innovative pharmaceuticals and non-innovative ones. Although the effect of introducing product patents in pharmaceuticals on the launch delay of new pharmaceuticals has been studied, no attention has been paid to the effects of the innovativeness of new medicines on the speed of launch. Based on innovativeness of new molecular entities (NMEs) classified in Lanthier et al. (2013), we take innovativeness of new medicines into account in our launch study and price study. Second, we examine whether or not there is evidence of differential pricing of pharmaceuticals, and here we differentiate between the pricing strategies of originator and of generic companies. Third, we analyse our research questions for different disease conditions, as well as countries' income levels.

Findings in this paper are summarised here. In the launch study, we find that the introduction of product patents has a positive effect on launch likelihood, especially for innovative pharmaceuticals, but this effect is limited in low-income markets. Launches of non-innovative medicines seem to be facilitated by the patent regime only in high income markets. Innovative pharmaceuticals are launched sooner than non-innovative ones irrespective of the patent regime in the local market. With regard to the second question of differential pricing of pharmaceuticals, we find evidence of differential pricing for both originator and generic products. Overall, originators differentiate by about 11% and generics by about 26%. Differential pricing is larger for pharmaceuticals to treat infectious diseases, particularly for HIV/AIDs medicines, than for non-communicable diseases. However, pharmaceutical prices are far from being fully adjusted to local income levels in either case. Compared to originator products, pricing of generics is more sensitive to whether the medicine is an innovative one or not, disease condition, local income level, and income distribution. The study also finds that competition, especially the within-molecule competition, can effectively drive prices down in both originator and generic markets.

This paper is organized as follows. Section 2 provides the background and the relevant literature for this study. Section 3 introduces the data used in our empirical research. Section 4 presents summary statistics of launch outcomes and prices from our data sets. Section 5 presents the empirical specification and results of the launch study. Section 6 presents the specification and results of the price study. In Section 7, we present other specifications done as robustness checks, and discuss sources of potential endogeneity in this paper. The last section resumes the conclusions of this paper.

[2] Throughout this paper we use the terms medicine, drug, and pharmaceutical interchangeably.

[3] IQVIA, previously IMS Health and Quintiles, (https://www.iqvia.com/de-de/about-us) is a global market research company in the business of selling health care data collected from around the world, including to pharmaceutical companies. Many health economists rely on this data for their analysis.

2 BACKGROUND AND RELEVANT LITERATURE

This section provides a brief explanation on the TRIPS Agreement in relation to pharmaceutical patents and surveys the most relevant prior work done on the research questions posed by us.

2.1 Pharmaceutical product patent and TRIPS

It is well-accepted by economists that patent protection is especially important for the pharmaceutical industry (A. Lopez, in WIPO, 2009).[4] Originator pharmaceutical firms file patent applications for a new compound at a very early stage in the research process, usually prior to the conduct of clinical trials. On average, it takes 8 to 12 years from the filing of a patent application to conduct clinical trials, to assess a candidate medicine's safety, efficacy, and quality, and to obtain market approval for a new medicine before its commercialization.[5] Only a small proportion of compounds involved in clinical trials is eventually approved for sale, and each new pharmaceutical product marketed is associated with millions of US dollars in R&D costs, including the costs of failed products.[6] A new drug is launched in a market only if the originator expects the market to be profitable. However, once a new medicine is marketed, it can be copied by other manufacturers through reverse engineering, especially if these are not otherwise technologically complex products, and those resulting generics can be sold much cheaper than originator products since generic firms have little R&D expenses. As a result, originators may lose the market and be reluctant to enter a new market that has potential generic imitators. Product patent protection prevents market entry of generic competitors before patent expiry, and thus the originator (or licensee) is the only supplier in the market for a limited period of time before the patent expires.

Though patent laws have a long history, the decision to either introduce a patent system or not used to be the preserve of sovereign decision making in each jurisdiction before the TRIPS Agreement. Prior to this agreement, the standards for patent protection varied across states depending on their domestic patent laws. Even in countries where patent protection was provided, the state could then choose to exclude pharmaceuticals (and other sectors) from patentability or only provide protection for the processes/methods of producing a pharmaceutical instead of for the final product. Wide variations in the strength of patent protection across markets were observed in 1980s[7], and there were concerns that insufficient protection of inventions could impede trade flows and slow down further investment in R&D activities. In the Uruguay Round of multilateral trade negotiations, protection of intellectual property rights was put on the negotiating table in 1986. Pharmaceutical patent protection was among the core issues in these negotiations.[8] The draft text of TRIPS released by the then Director General of GATT, Arthur Dunkel, at the end of 1991 as a part of the proposed compromise, already included the obligation to make patents available for all fields of technology

[4] See Lopez, A: "Innovation and Appropriability, Empirical Evidence and Research Agenda", available at http://www.wipo.int/edocs/pubdocs/en/wipo_pub_1012-intro1.pdf for a good summary of the literature. "The pioneer studies on patents and appropriability (Scherer et al., 1959 for the US and Taylor and Silberston, 1973 for the UK) showed that patents were important as a means to profit from innovation *only* in the pharmaceutical industry. Later on, Mansfield (1986) found – based on the firms' own answers – that only in the pharmaceutical and chemical industries a large number of innovations would not have been developed or introduced in the market without patent protection, although, at the same time, the survey showed that firms patented most of their patentable inventions. A similar conclusion had already been reached in Mansfield et al. (1981). The limited importance of patents for innovative firms received further confirmation in a study by Levin et al. (1987) who, in 1983, asked 650 R&D performing manufacturing firms in the US about their preferred methods to protect innovations. In 1994 a new study was made on a similar basis involving 1,478 US firms employing from 20 to more than 100,000 workers (Cohen et al. (2000)). A distinctive feature of these studies was that they included other appropriability means such as secrecy, lead times, moving rapidly along the learning curve and complementary sales, services and manufacturing facilities.

[5] See Office of Technology Assessment, 1993 available at http://govinfo.library.unt.edu/ota/Ota_1/DATA/1993/9336.PDF (see p. 83-84); European Commission, 2009; Sternitzke, 2010; Mestre-Ferrandiz, Sussex, and Towse, 2012; Wagner and Wakeman, 2016.

[6] The precise amount is controversial. In DiMasi, Grabowski, and Hansen (2016), the estimated R&D expenses per FDA approved drug is 2.56 billion USD (at 2013 current value), after taking costs of compounds abandoned in clinical trials into account. This estimation is based on a sample of 106 randomly selected drugs in 10 pharmaceutical firms. In Mestre-Ferrandiz, Sussex, and Towse (2012), R&D costs per approved drug is estimated as 1.51 billion USD at 2011 prices based on a confidential survey.

[7] This is recorded in MTN.GNG/NG11/W/24, p. 47 where WIPO noted that at least 44 countries, including developed countries, excluded pharmaceuticals from product patent protection as of May 1988, not counting those that disallowed mere mixtures of known ingredients.

[8] See Watal, J: "Patents. An Indian perspective" in *The Making of the TRIPS Agreement*, available at https://www.wto.org/english/res_e/booksp_e/trips_agree_e/chapter_16_e.pdf.

with few exceptions. This text underwent only small changes between 1991 and the final text of April 1994. Since the establishment of the WTO in January 1995, acceding WTO Members had to – with few exceptions – generally accept the provisions of all WTO agreements, including the TRIPS Agreement.

TRIPS requires Members to make available patent protection for inventions, whether products or a processes, with a term of protection that shall not end before 20 years from the filing date, although and assessing the validity of a patent continues to be left to each jurisdiction. While allowing certain exclusions from patent protection, TRIPS does not exempt pharmaceuticals from patentability (Article 27), and thus obliges the introduction of pharmaceutical product patents with a 20-year protection term for WTO Members. Since 1990, a number of countries have introduced patent protection for pharmaceutical products, a fact largely attributable – directly or indirectly – to this requirement in the TRIPS Agreement.

Pharmaceutical product patents were introduced in different jurisdictions at different time points. Many developed countries and some developing countries were already TRIPS-compliant by 1995, and most new members which joined WTO after 1995 applied TRIPS as soon as they joined. Transition or grace periods are provided in the TRIPS Agreement for developing countries and least developed countries (LDCs) to delay its implementation, particularly the obligation to provide intellectual property protection for pharmaceutical products. Developing country members were only allowed time up to January 2005 to protect pharmaceutical patents but were required to accept pharmaceutical product patent filing from January 1995 (the so-called mailbox system).[9] Currently only LDCs continue to be provided with this transition period up to January 2033, even while other TRIPS provisions need to be complied with by LDCs by mid-2021. Thus, by 2005, all WTO Members were meant to be compliant with TRIPS in this respect, except LDCs.

Debates over the impact of TRIPS on public health tend to focus on the lack of access to new, innovative drugs in poorer countries due to high prices. For most low and middle-income countries, the government or private health insurance (where it exists) covers a limited share of expenses for the purchase of needed medicines, if at all, and patients are thus more sensitive to the prices of new medicines. During the patent term, if the originator does not launch its medicine in the market or if the originator products are unaffordable due to high prices, patients who need the medicines may be left untreated or undertreated. Whereas if no patent existed in the market, these patients' health needs could possibly be met through affordable generics that are either produced locally or imported. Under the TRIPS Agreement, compulsory licences could be made available to third parties that are willing to produce or import these patented medicines, and this was clarified, along with additional flexibilities, through the Doha Declaration on the TRIPS Agreement and Public Health in 2001. Patent holders still have a right to be paid adequate remuneration for the generic products made under the compulsory licence.

2.2 Economic studies in patent and access to new medicines

The availability of product patents could play a determinative role in the decision of pharmaceutical companies to launch their new products in markets and to set or revise prices for these products over time. A product patent provides market exclusivity for patent owning companies, and in theory the profits generated by the product under patent protection creates incentives for originators to enter the market. On the other hand, a product patent blocks generic entry before patent expiry, and thus the drug is available on domestic market only if the originator launches it. In addition, lack of generic competitors may cause the drug to be less affordable even if it is launched. Although it is known that patents are uniquely important for the pharmaceutical industry, factors determining launch and price decisions in different markets are still open to empirical examination. In this section, we review previous studies on launch delay and price setting of new medicines, and we briefly present the research questions, methods, and findings of these studies. Most studies use data taken from IMS Health (now IQVIA) except Kyle (2006) and Kyle (2007) which use the Pharmaprojects database maintained by a UK consulting firm.

To begin with, we review studies in determinants of global diffusion of new drugs. Danzon, Wang, and Wang (2005) study how price regulation affects the launch delay of new drugs, using launch data in 25 countries from 1994 to 1998. Price regulation of each new product is proxied by the expected price, which is in turn constructed by average prices of drugs in the same therapeutic class

[9] https://www.wto.org/english/news_e/news15_e/trip_06nov15_e.htm.

of medicines. Using the Cox Proportional Hazard model, they find strong positive effects of higher expected prices (proxy for less price regulation) on the probability of launch. Findings in Danzon et al. (2005) are supported by Costa-Font, McGuire, and Varol (2015). Using a similar method and data, Costa-Font et al. (2015) examine the impact of market price on drug launches with a data set of 20 OECD countries plus South Africa from 1999 to 2008. Price regulation and launch is also examined in Kyle (2007). Using launch data in 28 countries from 1980 to 2000, she finds that a product initially launched in a price-controlled country would eventually launch in a smaller number of countries globally and that price control causes launch delay of new drugs. Kyle (2006), using a smaller sample of G7 countries and the discrete hazard model, finds that the launch likelihood of a new drug in a market depends largely on the originator's familiarity with that market. For example, a new medicine is more likely to be launched in markets where its originator is marketing other medicines. Voral, Costa-Font, and McGuire (2012) study the impact of the regulatory environment more broadly on diffusion of new drugs. They analyse launches from 1960 to 2008 in OECD countries with non-parametric and semi-parametric methods and focus on effects of two regulatory changes, viz. the US Hatch-Waxman Act in 1984 and the establishment of the European Medicine Agency in 1995. They find that launch delay has become shorter over time, because implementation of these new policies reduces transaction costs by harmonizing market authorization, strengthening intellectual property protection, and reducing geographic barriers. In sum, the five papers introduced above show that regulatory environment, especially price regulation, plays an important role in launch decisions of innovator companies. However, patents are not discussed as an explanatory variable in this context.

The two important studies that take patents into account in companies' decisions on launch of pharmaceuticals in different markets are Kyle and Qian (2014) and Cockburn, Lanjouw, and Schankerman (2016). Kyle and Qian (2014) examine the effects of patent protection on the speed of launch, price, and quantity in 59 countries. Launch data from 1990 to 2013 is used. Using a discrete time hazard model and using patent protection data by molecule in each country, they find that patents facilitate launches of molecules in the local markets. Cockburn et al. (2016) study the impacts of both price control policies and patents regime on launch decisions. They use launch data covering 76 independent markets from 1983 to 2002 and adopt a parametric hazard model with Weibull distribution. The patents regime is measured at the country-year level, and a set of dummy variables are used that specify the term of protection (short, medium, or long) and the type of protection (process or product). Findings in Cockburn et al. (2016) are robust to endogeneity examination of policy regimes, and they conclude that price regulation delays launch, while longer and more extensive patent rights accelerate it. In both papers, demographic features such as GDP per capita and population are controlled. Both these papers focus on earliest access to new pharmaceutical and thus define a local launch as the first appearance of a new drug in a given market without distinguishing between whether it is launched by the originator firm or the generic firm.[10][11] We apply the same definition of launches in our study.

Apart from researching the question of launch delay, pricing in the pharmaceutical sector across countries has also been well studied. Danzon and Furukuwa (2008) present the stylistic facts on price differentiation across 12 countries, viz. France, Germany, Italy, Spain, UK, US, Canada, Australia, Japan, Brazil, Chile, and Mexico in 2005, and they find that compared to the prices in the United States, originator products are usually cheaper in other countries, while generics are more expensive in these countries. In Flynn, Hollis, and Palmedo (2009), the hypothesis posed is that the monopolistic pharmaceutical firms will price products differently according to income inequality in local markets. Through theoretical modelling it is shown that in the case where income distribution in the local economy is unequal, the firm will maximize its revenue by selling a smaller quantity to the very rich at a higher price, and therefore it has no interest in differential or tiered pricing. With a focus on HIV/AIDS, TB, and malaria medicines, Danzon, Mulcahy, and Towse (2015) analyse determinants of ex-manufacturer prices for originator and generic pharmaceuticals across countries using a dataset in 37 countries from 2004 to 2008. They provide evidence for the hypothesis in Flynn et al. (2009) that income inequality does contribute to relatively high drug prices. Besides, they find that additional generic competitors can only weakly reduce prices of originator products. Kyle and Qian (2014) examine the impact of patent protection on price and quantity using a dataset

[10] In Kyle and Qian (2014), "We simply estimate whether countries have earlier access to innovations when patent protection exists (or ever existed) there, without distinguishing whether the originator or imitators enter first." See page 10.

[11] In Cockburn et al. (2016), "A launch is defined as the first appearance of a drug in a given country, whether in proprietary or generic form, and the launch lag is the time elapsed since the first launch of the molecule in any country." See page 149.

of 59 countries from 2000 to 2013 using IQVIA data, where patent expiry dates at molecule-country level are examined and the price of each drug is normalized to standard units (smallest dose). Patent status is categorized into three groups, viz. no patent, on patent, and expired patent. Pooling originator and generic products, they find that, patented molecules have higher prices but higher quantities as well, and that the price premium is smaller in poorer countries. Endogeneity of patent status is addressed in the paper with instrumental variables.

3 DATA

This section will cover both the type of data used and the adjustments made to it in order to find the best proxies for the explanatory variables used in the empirical models on launch and price.

3.1 Pharmaceutical data

The aim of this study is to provide empirical evidence on impacts of product patent on accessibility of the most innovative pharmaceuticals. We distinguish between innovative drugs and non-innovative drugs according to their innovation categories constructed by Lanthier et al. (2013). Lanthier et al. (2013) propose three distinct sub-categories of new molecular entities (NMEs) to measure the degree of innovativeness of new pharmaceuticals, namely, first-in-class, advance-in-class, and addition-to-class. First-in-class drugs are innovative, because each presents a new pathway for treating a disease. Advance-in-class drugs are defined as drugs that are not first-in-class but receive a priority review designation from USFDA, which is reserved for medicines that potentially offer major advances in treatment. The remainder of drugs are classified as addition-to-class drugs. Lanthier et al. (2013) examine all 645 novel therapeutic products approved by USFDA from 1987 to 2011, and they list the innovation category of each NME in the appendix of the paper. In our study, we define that molecules in both first-in-class and advance-in-class categories are innovative pharmaceuticals, and those in addition-to-class category are additional or non-innovative pharmaceuticals.

Our pharmaceutical data is provided by IQVIA, previously known as IMS Health or Quintiles. IQVIA's proprietary MIDAS® database is an analytics platform that enables analyses on sales data from 70 markets in a standardized and comparable way. It allows researchers to understand markets down to the most granular level in terms of therapy areas, manufacturers, products and packs, formulations and ingredients, innovative brands and generics, and so on.[12] For this study we used the following data elements – molecule, brand, sales quantity (in terms of kilogram or International Unit) estimated sales price, and launch date and the following classification – Originator/Licensed Product versus Other Brand or Unbranded. IQVIA collects sales audits in selected countries through its sales audits that are derived from a mix of wholesaler, manufacturer and outlet level invoices, and the proportions in each audit vary by country and distribution channel. IQVIA standardizes these data and categorizes the products and sales according to a number of different classifications, some widely known such as EpHMRA ATC, and others that are proprietary to IQVIA, such as the National Form Code (pharmaceutical formulation description) and Standard Unit (a measure of volume).

In the IQVIA database, products of each molecule can be marketed under four types of brands, viz. Original Brand, Licensed Brand, Other Brand, and Unbranded. A product must meet two requirements to be defined as an originator or a licensed product: (1) it currently has or used to have a NME patent, and (2) it is being manufactured and/ or marketed by the originator company or the licensee, irrespective of whether the molecule patent has expired or not. We define products under Original Brands or Licensed brands as originator products, and the remaining products in each molecule market are classified as generics regardless of whether these are branded or not. For each medicine of interest, we collect sales data for both the originator and generic products. Among 645 NMEs examined in Lanthier et al. (2013), 578 molecules have original or licensed brands in the IQVIA database, and the rest have never been patented in any of the market in our sample.[13] Since patents are of interest to us as an explanatory variable, we restrict our sample to the 578 products which are subject to product patent. These consist of 307 innovative pharmaceuticals and

[12] IQVIA MIDAS website: https://www.iqvia.com/solutions/commercialization/geographies/midas.

[13] For the products having no molecule patent, they may have method patents. However, the product only having method patent cannot be classified as original or licensed products in IQVIA database.

271 non-innovative/additional pharmaceuticals. Details of our pharmaceutical sample are presented in Table 1.

In this paper, we have collected data from 70 markets in the IQVIA database, including 26 high-income, 19 upper-middle-income, 19 lower-middle-income, and six low-income economies according to the World Bank classification in 2000. In two cases countries are aggregated at regional level: French West Africa consists of 12 countries, namely Benin, Cote d'Ivoire, Burkina Faso, Cameroon, Congo, Gabon, Guinea, Mali, Niger, Senegal, Chad and Togo; and Central America, consists of six countries, namely Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica and Panama.[14] Detailed market information is given in Table A3 in the Appendix.

3.1.1 Launch data

We extract the launch date of each molecule in markets where the molecule is sold. A launch date is defined as the time at which a pharmaceutical is first sold in a local market, irrespective of whether it is marketed by the original patentee/licensee, or a generic firm. For each pharmaceutical in each market, the launch date is determined according to following rules given data availability in our data set:

1. If originator products are on the market where there is no generic product, we take the month in which originator products first appeared on the market.
2. If generics are on the market where there is no originator product, we take the month in which the generic products first appeared on the market.
3. If both originator and generic products are present on the market and the first appearance months of both are specified, we take the earlier month in which the products first appeared on the market.
4. If both originator and generic products are present on the market but only the first appearance month of originator products is specified, we take the month in which the originator products first appeared on the market.
5. If both originator and generic products are present on the market but only the first appearance month of generics is specified, we code the launch date as missing, and observations in this case are dropped from non-parametric and semi-parametric analyses.

Based on local launch dates of each molecule, we define the global launch date as the earliest launch date of the molecule anywhere in the 70 markets i.e. 68 countries and two country groups for which we have data. The number of months between the global launch date and the local launch date is defined as the launch delay of the molecule in the given market. Initially, we had launch records of 578 molecules[15] in our sample, but 22 of them were first launched somewhere in the world before 1980 probably as other versions. Since all products were approved by USFDA from 1987 to 2011 and these 22 products were launched far too early elsewhere for these to be credible, we drop these products from the launch sample. As a result, there are 556 pharmaceuticals in launch analyses. The distribution of global launch years of these 556 molecules is presented in Figure 1, where most new pharmaceuticals were introduced into markets after 1990. The number of total launch opportunities for 556 molecules in 70 markets is 38920. Among them, we collected 24,730 launch records with specific launch date and 382 launch records whose launch dates are unspecified. These 382 molecule-market combinations are unavailable in survival analysis in the following sections. For the remaining 13808 molecule-market combinations, launch has not taken place yet by 2018q1. In regressions on launch likelihood, we further restrict the sample to 540 molecules due to missing disease burden variable of 16 molecules (See Section 3.4 of this paper for the part on disease burden data).[16]

[14] For the two country groups, their income classification is determined by population weighted GDP per capita and the threshold of each income level given by the World Bank.

[15] If a product was no longer on local market since 2006, its launch record may not be retrieved from the IQVIA database. Among the 587 molecules, we only found originator launch records of 550 molecules in the United States, which could result from the rest 37 molecules were no longer on the US market since 2006. We add the launch date of these 37 molecules in the originator launch data set according to their FDA approval date.

[16] In regression, we only consider 540 molecules whose disease burdens can be specified. There are 37800 launch opportunities in total. Among them, 23998 launches have taken place with specified launch

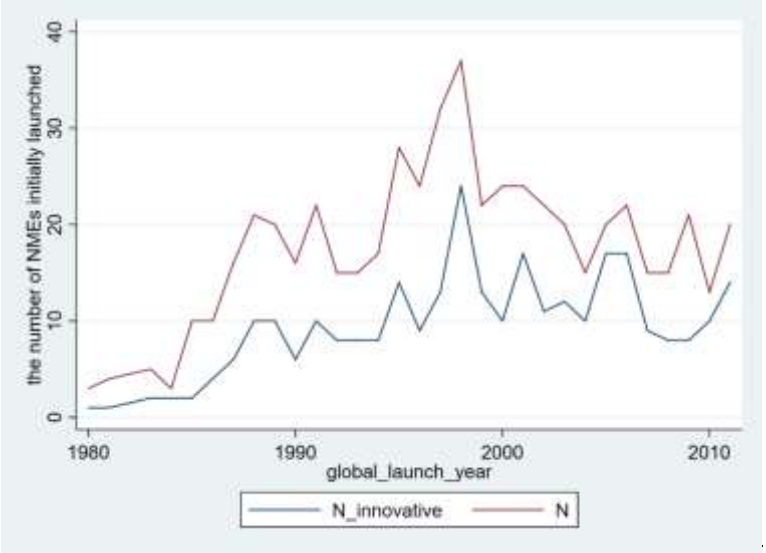

Figure 1: Time distribution of global launches for 556 NMEs

3.1.2 Price data and caveats

For the price study, we use estimated ex-manufacturer prices in US dollar from 2007 to 2017. For each molecule present in each year on each market, we obtain its ex-manufacturer price per kilogram or per international unit [17] by originator and generic products. Among the 578 molecules, 573[18] of them had originator products on the market during our study period, and 504 of them had generics sold somewhere in the world.

The IQVIA price data set consists of estimated ex-manufacturer prices. IQVIA collects information on a sale price at a particular level within the pharmaceutical supply chain. Depending on the country, this can be a manufacturer or wholesaler price list, a weighted average manufacturer or wholesaler sale price, or a regulated out-of-pocket or reimbursement price. On the basis of a market survey, the average mark-up from manufacturer to wholesaler to outlet is calculated. This average mark-up is then applied to the price collected for each product collected so as to estimate ex-manufacturer price. In MIDAS the same price and discount is applied to all products irrespective of the channel. Thus, for example, in those countries where IQVIA relies on reimbursement or price list information, this information is applied to both hospital and retail products. Similarly, even if it is generally acknowledged that discounts are often larger for generic products than for branded or on-patent medicines, no allowance was made for this in this study.

Given this knowledge on how ex-manufacturer prices are estimated, we address the limitations of the IQVIA price data here. Firstly, this price is different from the price on market for consumers. Margins added by wholesalers, retail pharmacies and any other elements of the distribution chain to the patient are not captured, nor are any other tariffs or taxes. In many countries, these are regulated margins. In some countries, they are not. A certain level of mark-up added by distributors is the necessary cost of delivering medicines to patients safely, securely, and reliably by commercial enterprises. However, in some countries where distribution margins are unregulated and/or distribution is inefficient and involves many actors, mark-ups can substantially increase the cost of

dates. There are 357 launch records without specified launch date, and they are excluded from further analysis. There is no launch happened to the rest 13445 launch opportunities.

[17] International units (IU) are used to quantify vitamins, hormones, some medications, vaccines, blood products, and similar biologically active substances, which varies based on which substance is being measured. There are 17 pharmaceuticals out of 578 whose measurement unit of price is international unit. They are CALASPARGASE PEGOL, DALTEPARIN SODIUM, DANAPAROID, ENOXAPARIN SODIUM, EPOETIN ALFA, IMIGLUCERASE, INSULIN ASPART, INSULIN DETEMIR, INSULIN GLARGINE, INSULIN GLULISINE, INSULIN LISPRO, INTERFERON ALFA-N1, INTERFERON ALFA-N3, INTERFERON BETA-1A, INTERFERON BETA-1B, INTERFERON GAMMA-1B, and VELAGLUCERASE ALFA.

[18] For these five molecules, there was no sale under original or licensed brand in our sample since 2007, viz. CERIVASTATIN, SAMARIUM (153SM) LEXIDRONAM, TOSITUMOMAB IODINE-131, VALRUBICIN, and GREPAFLOXACIN.

medicines to the patient.[19] It should be noted also that the prices may or may not contain VAT or other taxes (sometimes applied at regional level) depending on the practice in the country. Thus, differences in distribution margins, tariffs or taxes were not taken into account in this study.

In addition, while average weighted sale price may contain some information on discounts, there are also non-publicly available discounts or rebates that are not included in this price, meaning the actual price the manufacturer realizes is in fact lower. These non-publicly available rebates/discounts can be substantial. For example, it is now estimated that in the US the average share of the price that goes to private insurers, pharmacy benefit managers and other intermediaries is 41%.[20] No estimate is made to account for such non-publicly available rebates/discounts in this study.

In spite of these measurement problems, this price data set is the most comprehensive one for economic analysis of pharmaceuticals and is used by most economists doing similar studies.[21]

3.1.3 the Anatomical Therapeutic Chemical (ATC) class

We link each molecule to a unique therapeutic class, known in as the Anatomical Therapeutic Chemical (ATC) class. In the ATC classification system, the active substances are classified in a hierarchy with five different levels according to the human organ or the system on which they act and their therapeutic, pharmacological and chemical properties. ATC 1 (one-digit ATC code) is the most aggregated level, while ATC 5 is the most specified level, which is equivalent to the active substance itself. We take level 4 in each ATC class (ATC4) as being representative of the therapeutic use for the product and the level of competition facing each molecule in each market. Since level 4 has the next lowest level of aggregation, molecules within the same ATC 4 class are expected to treat the same or similar disease condition and so be able to substitute each other to some extent.

ATC 4 classification of each molecule and the corresponding disease category of each ATC4 class are available in the data provided by IQVIA. With the ATC4 class known, we link each molecule to a disease condition and obtain the disease burden data for each product in each market. It can happen that a particular medicine is used to treat several disease conditions. In the case where a molecule is classified into multiple ATC4 classes (for example, the antibiotic ciprofloxacin can be classified as an anti-infective drug for eye and ear infections, as well as like an oral fluoroquinolone), we assign this molecule into the class which takes the largest share of global quantity sold in Standard Units (SU).[22] For the few products whose treatment is unspecified by ATC 4 match, we found the disease category by internet search (see more details discussed in Section 3.4 below). Table 1 presents the number of products in each disease category.

We also construct competition indicators by molecule and by ATC group. The two competition indicators are the number of brands by molecule and the number of brands in ATC4. Here brands refer to either original brands, licensed brands, generic brands, or unbranded generics. These data are available in each market from 2007 to 2017. Though we assign one unique ATC4 category to each pharmaceutical to link disease category based on global quantity sold, we link the ATC4 classification of each molecule on a domestic basis when constructing competition indicators. This variable provides us with a more accurate measure of competition intensity in the local market. For molecules classified into multiple ATC4 classes in one market, we take the ATC4 whose count of brands is the maximal for the molecule.[23] Products in the same ATC4 class are likely to treat the same disease condition, even though they may not be perfect substitutes of each other. Thus, conditional on substitutability, we expect increasing the number of brands per molecule could

[19] Taken from a presentation made by Ms. Sarah Rickwood, Vice President IQVIA at the WHO, WIPO, WTO Symposium, 2017, available at http://www.who.int/phi/2-SarahRickwood.pdf.

[20] See Sood, N et al. "Follow The Money: The Flow Of Funds In The Pharmaceutical Distribution System", available at https://www.healthaffairs.org/do/10.1377/hblog20170613.060557/full.

[21] WHO and Health Action International are building a publicly available medicine database for selected medicines, but it does not have adequate coverage either geographically, therapeutically or chronologically for our purposes.

[22] The standard unit is defined as the smallest dose of each presentation of pharmaceuticals, e.g., 5ml liquid, per tablet or per vial.

[23] For example, in 2007, products of Ciprofloxacin can be classified in both J1G1 and J1G2 classes in a market, and products in J1G1 has five brands and that in J1G2 has only two brands. In this case, we take five as the brands of Ciprofloxacin by ATC4 in 2007 in the market.

intensify price competition and drive the price down. Another indicator of competition is the number of brands in each molecule market, which we take as the existence of an absence of patent protection. This competition measure indicates even more competition for the molecule in question as each brand is a perfect substitute by definition.

3.2 Patent data

We have two patent indicators used in the launch study and the price study respectively. In the launch study, we aim to examine effects of the introduction of product patents at national level on the probability of launch in that market, and thus we construct one binary indicator of product patent in pharmaceuticals. We only consider the product patent regime, because process patents in pharmaceuticals cannot guarantee market exclusivity and thus pharmaceutical firms may have limited incentive to launch a new medicine on the basis of the mere introduction of process protection for pharmaceuticals. Besides, this indicator does not take the length of protection into account, in view of the fact that WTO Members generally provide 20-year protection at the point of extending patent coverage to pharmaceutical product.

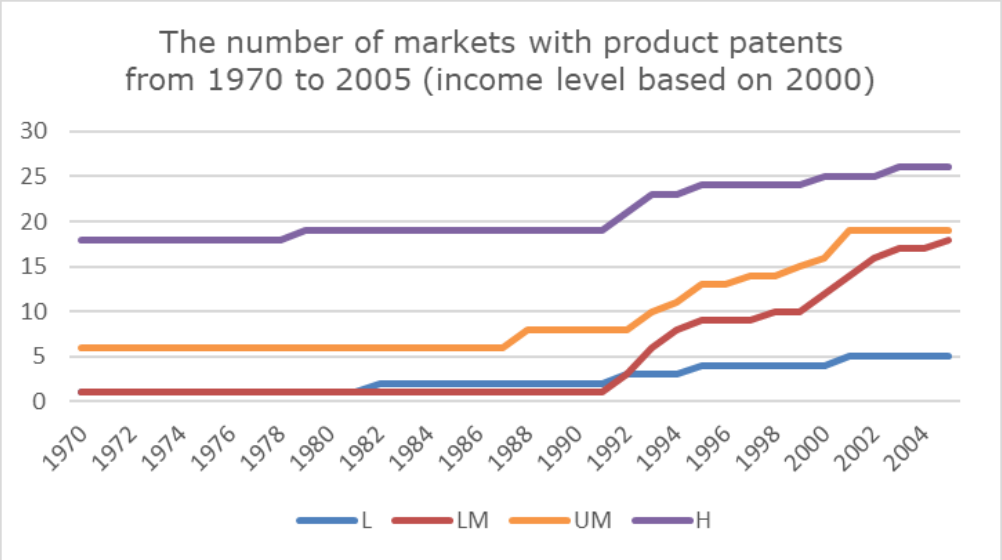

Figure 2: The number of markets with product patents in pharmaceuticals by year

We did our own research to track the change in the patent regime in each market. We define the year in which product patent was introduced as the year in which a product patent application in pharmaceuticals can be filed in the market. We also try to control the enforcement of protection, and we consult the patent index in Park (2008) and Liu and La Croix (2015). However, neither index is made annually nor focused on the introduction of product patents for pharmaceuticals. Therefore, we do not take IP enforcement into account in this study. Figure 2 presents the number of markets which have available product patent in pharmaceuticals from 1970 to 2005. After 2005, no market in our study changed its rules on patentability of pharmaceuticals in our sample (although judicial decisions naturally lead to evolution in how statutory patentability standards are applied). Since 1990, a number of markets – at different income levels – viz. low (L), low-middle (LM), Upper middle (UM) and High (H) income levels - have introduced product patents, which can be largely attributed to the requirement of TRIPS.

We match launch data and patent information in the following way: a molecule is patentable in a market if product patents have been available for pharmaceutical products at least ten years prior to the global launch of the molecule. We use ten-year lag here, because it takes ten years on average from the date of filing a product patent application to obtain marketing approval for the product in a market.[24]

[24] Deduced from a number of studies known to the authors, including Grabowski, H. and M. Kyle (2007): Generic Competition and Market Exclusivity Periods in Pharmaceuticals, *Manage. Decis. Econ. 28: 491-502*. See also European Commission (2009), page 339.

The other patent variable is provided by IQVIA, where date of protection expiry is available in 59 markets for at most 481 molecules including 16 molecules whose disease burden cannot be determined. This data set is unbalanced in that the range of molecules with patent status varies across these 59 markets. For the market-molecule combination without patent information, their patent status could be non-patented, but it is also possible that they are missing because their patent information has not been found. For the market-molecule combination with patent status, either the molecule is subject to an active protection or the protection of the molecule has been expired in the local market. We construct one binary indicator of protection expiry based on this data set, which is equal to one in the given year after expiry in the local market. In the case where there are multiple protection expiry dates for one market-molecule combination, we take the latest one.

It should be noted that IQVIA does not specify the type of protection: this could be product patent protection, process patent protection, data exclusivity, or other forms of market exclusivity.[25] As noted earlier, certain types of protection cannot block generic entry. As shown in Table 2, among all generic price observations where date of protection expiry is available for their market-molecule combinations, 12.7% (1-0.873) were on market before the end of protection, which suggest that protection in the data set may not necessarily mean market exclusivity. It is one of the reasons why we chose not to use IQVIA protection data in our study.

3.3 Socio-economic variables

We take socio-economic variables into account in both the launch study and the price study. These variables are population, GDP per capita (measured in current USD), Gini coefficient, life expectancy, and health expenditure as a percentage of GDP. They are taken from the Word Bank website. For the two country groups, namely Central America and French West Africa, we take the population weighted average of values in their member states by year. For health expenditure as a percentage of GDP, we use GDP of each member state as the weight and construct the weighted average. Population of each country group is the sum of populations of member states in this group. We also employ income level of countries or regions classified by the World Bank. For these two country groups, their income group is determined by comparing their GDP per capita (calculated as the population weighted average) and the threshold of each income group given by the World Bank.[26]

For the missing values of these five variables, we fill in all missing values prior to the first observation with the value of the earliest observation, and then we fill in gaps between two observations with the former observation. Table 2 presents summary statistics of socio-economic variables from 1980 to 2017 without backward filling. As shown in Table2, missing values concentrate on Gini coefficient and health expenditure as a share of GDP. Health expenditure is available since 2000, and Gini coefficient is estimated only occasionally in each market, though its availability is better for some markets in recent decades. We understand that backward filling may cause problems since those values are not predetermined. However, if we only kept observations having complete covariates, observations in early periods would be dropped and the sample would be severely biased towards developed markets. Due to sample selection issues, we chose to take the risk of backward filling.[27] Apart from missing values which could be filled in, the Gini coefficient is unavailable in seven markets in our sample, viz. Hong Kong, Kuwait, New Zealand, Puerto Rico, Singapore, Saudi Arabia, and United Arab Emirates. Therefore, these seven economies are excluded from regression analysis once we include Gini coefficient as a regressor.

[25] It is obligatory under TRIPS to protect test data protection for pharmaceuticals involving a new chemical entity against unfair commercial use and disclosure but many countries go further and grant market exclusivity for new pharmaceuticals, generally for a fixed period of time ranging from 5-12 years from the date of marketing approval.

[26] For the Central America, it was in lower-middle-income group during 1987-2011, and it was in upper-middle-income group after 2012. For the French West Africa, it was in lower-middle-income group during 1987-1992, and it was in low-income group after 1993, except in 2008 when it was classified into lower-middle-income group for one specific year only.

[27] We use backward filling more often in the launch data set. In the price study, only Gini coefficients of the five markets are backward filled, viz. China, India, Indonesia, Japan, and Lebanon. The fill-in proportion is less than 2.8 percent in datasets for price regression.

3.4 Disease burden

To capture the disease burden in each market, we use Disability-Adjusted Life Year (DALY) data published by the World Health Organization and link DALY to pharmaceuticals according to their uses. DALY is the number of years lost of healthy life, which consists of the loss due to deaths in population and disability for people living with conditions. We merge three waves of DALY in 2000, 2010, and 2010 by market and by disease category of each molecule in our dataset. There is no DALY data available for Hong Kong and Puerto Rico in the original data source. DALY of the two country groups are calculated as the sum of values of their member states. Since DALY is not published annually, we fill in missing values in the gap with the earlier observation in each market, and for years prior to 2000, we use DALY data in 2000. For markets whose malaria data is missing[28], we fill in the minimal value of malaria burden in that wave since those markets are not in endemic areas. We classify all conditions into 22 categories and assign each pharmaceutical into one of them. To determine the uses of each pharmaceutical, we consult IQVIA for ATC4 classification of each product and the corresponding uses of drugs in each ATC4 group. For medicines in ATC4 groups which are linked to unspecified conditions[29], we specify the uses of each product by internet search and link each pharmaceutical to a disease category based on its target patients.[30]

Table 1 presents the distribution of 578 molecules by disease burden, and Table 2 provides summary statistics of DALY. As shown in Table 1, in either innovative or non-innovative pharmaceutical group in our sample, most medicines are used to treat non-communicable conditions, and only less than one sixth (95 out of 578) of all pharmaceuticals are infectious diseases' medicines, which reflects the healthcare needs in the U.S. and other high-income markets as all products in our sample are USFDA approved where the incidence of infectious diseases is low in populations. Among 95 infectious diseases' medicines, 25 products are used to treat HIV/AIDS related conditions, and four products are for malaria or TB. Most HIV/AIDS, malaria and TB pharmaceuticals are innovative based on the classification in Lanthier et al. (2013). Among 38 products used to treat "other infectious diseases", many are broad spectrum antibiotics, and their corresponding disease burden consists of sexually transmitted diseases (excluding HIV) and other unspecified infectious diseases. We also notice that pharmaceuticals for neglected tropical diseases take a very small proportion in our sample with only five products. Among 467 medicines for non-communicable conditions, anti-neoplastic (including cancer) medicines take the largest share, and 89 out of 111 anti-neoplastic medicines are innovative pharmaceuticals. The second largest group of non-communicable conditions' medicines is cardiovascular medicines with 84 products, although the majority of them are non-innovative. Table 1 also shows that there are 16 out of 578 products developed as anaesthetics, contraceptives or antidotes. These molecules are dropped in regression analyses since we find no appropriate DALY to link them to.

4 SUMMARY STATISTICS

4.1 Summary statistics of launch study

We begin with summary statistics on the extent and the speed of launches. We collect 25112 launch records for 556 molecules in 70 markets, which takes 64.5%[31]of potential launch opportunities. Figure 3a and Figure 3b present the number of molecules launched in each market by firm type. In more than 90% of cases, originator products entered markets before generic entry. In a few exceptional markets like India and Bangladesh, generics contributed greatly to access to new

[28] There are 44 markets whose malaria disease burden is missing in at least one wave. They are Argentina, Australia, Austria, Belgium, Bulgaria, Canada, Chile, Croatia, Czech, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Japan, Jordan, Kazakhstan, Kuwait, Latvia, Lebanon, Lithuania, Luxembourg, Netherlands, New Zealand, Norway, Poland, Portugal, Romania, Russia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tunisia, Turkey, UAE, UK, US, and Uruguay.

[29] We firstly try to link each ATC4 to a disease category based on information from IQVIA. Then, we further specify uses of pharmaceuticals whose ATC4 classes are linked to any of the following categories: Other and unspecified noncommunicable diseases, Other and unspecified infectious and parasitic diseases, Other and unspecified diseases/conditions, and Unspecified mental & behavioural disorders and neurological conditions. We manually specify the uses of 160 products out of 578.

[30] In most cases, the condition of the product to treat is consistent with the main condition of the patient. However, in a few cases, where the product is developed for a specific condition in a specific group of patients, we link the product to DALY of the main condition of the patients. For example, Cidofovir (trade name: Vistide) is a medicine used to treat cytomegalovirus (CMV) retinitis in people with AIDS, and thus we link Cidofovir to HIV/AIDS instead of sense organ disorders.

[31] 0.645 = 25112/38920

pharmaceuticals instead of originator products since, for a long period in our data set, product patent protection for pharmaceuticals was not introduced in these markets.

Up to the first quarter 2018, we observe a large discrepancy of availability of new pharmaceuticals across markets. Richer regions, where healthcare systems and patent regimes are well established in general, tend to have more original medicines available in our sample. This discrepancy should be interpreted carefully. One reason is that all medicines in our sample are USFDA approved and thus these may be biased towards health needs of developed markets. Secondly, the gap of launches across markets may result from underestimation of launches in certain markets where raw data is collected in either hospital[32] or retail sector[33] instead of both. We present market information in Table A3.

Table 3 shows launch outcomes by patent status and by income level. Patentability is a determinative factor for originators to make product launch decisions in different markets. Compared to markets without a patent regime, high-income and middle-income markets with product patents (at least ten years prior to the global launch of the pharmaceutical) have more products launched within ten years from the date of the global launch. It also takes shorter time to have one quarter of new pharmaceuticals launched in markets with the patent protection. However, in low-income markets, introducing patents in pharmaceuticals did not facilitate launch of new pharmaceuticals, probably because the patents regime blocked potential generic launches on which these markets used to earlier rely upon. The speed of launch and the fraction launched are also positively correlated with local income level, which suggests that patients in richer markets not only can access new pharmaceuticals sooner but also have a larger variety of new medicines to choose from.

4.2 Summary statistics of price study

In this subsection, we present summary statistics of pharmaceutical prices across markets. Our price data is measured in USD from 2007 to 2017. Depending on the nature of active substances, the measurement unit is either kilogram or international unit. There are three difficulties to directly construct a pharmaceutical price index by market. Firstly, the number and composition of launched pharmaceuticals varies by market. As discussed in Section 4.2, high-income markets have more medicines available in our sample. Secondly, the price of different medicines differs greatly. The standard deviation of pharmaceutical prices is shown in Table 2, which is huge. Thirdly, the daily dose and the duration of treatment varies by pharmaceutical. Without quantities sold by medicine as weights, we cannot link the unit price to pharmaceutical expenses. Given the aforementioned three points, the simple average of available prices by markets cannot provide us with any representative information on pharmaceutical price levels. As a result, we focus on within-molecule comparison.

We construct a ranking system across markets to show which markets are most likely to have high-priced medicines and which markets are most likely to have low-priced medicines. The detailed steps to construct rankings are described here. Firstly, for each molecule in each year, we rank prices of the molecule across all available markets. Then we obtain the five markets having the highest-five prices in each year and other five markets having the lowest-five prices of this medicine in each year. In the case where a molecule was available in fewer than ten markets in one year, price observations containing this molecule-year combination were ineligible for ranking and these were dropped. Secondly, we apply the first step to all eligible molecules in each year from 2007 to 2017, and obtain the price ranking of each market for each molecule-year combination. Thirdly, we sum up the number of price observations, the number of times the highest-five prices of pharmaceuticals appear, and the number of times the lowest-five prices of pharmaceuticals appear counted over all eligible molecule-year combinations. Lastly, we normalize the counts of highest-five prices and that of lowest-five prices to the number of eligible price observations by market.

We present the top 20 markets which have the largest share of the highest-five-priced or the lowest-five-priced originator products in Table 4a. As shown in Table 4a, pharmaceutical prices of

[32] Mainland China is the only market where data is collected only from hospital sector.

[33] There are 27 markets where data is collected only from retail sector, including Algeria, Argentina, Bangladesh, Brazil, Central America, Chile, Colombia, Dominican Republic, Ecuador, Egypt, Estonia, French Western Africa, Greece, Jordan, Kuwait, Latvia, Lebanon, Luxembourg, Mexico, Morocco, Netherlands, Pakistan, Peru, Saudi Arabia, Tunisia, UAE, and Venezuela. See Appendix for more details.

originator products tend to be high particularly in the U.S, Puerto Rico, Japan, and Latin American markets, while developing countries such as Turkey, India, Pakistan, Bangladesh, and Egypt are most likely to have low-priced originator medicines. Rankings in Table 4.1a are made based on absolute prices of originator products in USD. However, we are not only interested in prices, but also in the local affordability of these new medicines. To this end, we construct another ranking based on the income adjusted price, which is the ratio of the absolute price to GDP per capita of the economy in the current year.[34] Constructing the income adjusted price, we repeated the procedures as above, and the top 20 markets having the largest share of high-priced and low-priced originator medicines are listed in Table 4b. Taking income into account, we find that expenditures on originator pharmaceuticals take a larger share of income for people living in low-income and lower-middle-income markets than those living in richer markets. To summarize findings in Table 4a and Table 4b, we conclude that though originator products are probably cheaper in developing country markets, new medicines are still less affordable for people in poorer countries than in other countries.

Comparison of generic prices across markets are presented in Table 5a and Table 5b, where rankings are similar to the corresponding list of originator products. Income is the dominant factor of affordability of new medicines, either originator products or generics. Noticeably, we also find that New Zealand and the Netherlands have a large share of relatively low-priced generics, though originator products are not cheaper there than in other markets. In addition, prices of most originator products are high in the U.S. compared to other markets, but generics are not priced that high compared to prices elsewhere, especially after taking income into consideration.

5 LAUNCH STUDY

5.1 Specification of launch study

Since we base ourselves on Lanthier et al. (2013), we focus on pharmaceuticals which were approved by the USFDA from 1987 to 2011 and whose global launch took place in or after 1980. Because the observation period is limited and potential launches in the future cannot be observed in our sample (i.e., censored observations), the average launch delay cannot be calculated directly. Instead of estimating the average of launch delay, we apply methods in survival analysis and estimate launch likelihood as time goes by since the date of global launch. In this subsection, we introduce the specification used to estimate the impact of the introduction of product patents in pharmaceuticals on the probability of launch.

Our specification is based on the Cox Proportional Hazard model. The advantage of the Cox model is that estimation of coefficients is possible without making any assumption on the shape of hazard function, and we adopt the Cox model because we do not want to take the risk of making wrong assumptions on the hazard function. The specification equation is shown in Eq(1), where i indexes market, j indexes the particular pharmaceutical, and y indexes year. Taking socio-economic variables and disease burden ($\mathbf{x}_{ijy}$) into account, we aim to estimate marginal effects (β_p) of the introduction of product patents in pharmaceuticals on the likelihood of launch. Innovativeness of pharmaceuticals and the interaction term of innovativeness and patentability are also considered in Eq(1). $h(t|\mathbf{X}_{ijy})$ is the hazard function, representing the likelihood that pharmaceutical j is launched in market i in year y after time t which is the time since the global launch, this being conditional on all variables $\mathbf{X}$. $h_0(t)$ is called baseline hazard, which is the value of hazard function when all independent variables are equal to zero. In order to control for unknown episodes in the disease condition or year, we introduce ATC1 fixed effects and year fixed effects by adding dummies as shown in Eq(1). As in Cockburn et al.(2016), we take ATC1 instead of a less aggregated level, because ATC1 classifies 14 therapeutic groups based on organ systems on which medicines act and the therapeutic, pharmacological, and chemical properties of medicines, which is sufficient to capture heterogeneity of medicines used to treat different categories of diseases. Also, we want to keep enough variation within each therapeutic group for identification. To capture long run institutional heterogeneity across markets which affects the probability of launch as well as the timing of introducing product patent, we apply market fixed effects by stratification, i.e. each market i has its own baseline hazard function, and thus the probability of launch can be different across markets after time t since the global launch of the product, even if these markets have identical values of independent variables. To interpret regression results, a positive coefficient represents a positive effect of corresponding

[34] We also made the ranking based on PPP GDP per capita adjusted prices, which is highly similar to results using GDP per capita adjusted prices, and therefore we do not show the table here.

independent variable on the probability of launch. For example, if β of x is 0.2, we can interpret it as one unit increase in x increases the probability of launch by 22.14%, because exp(0.2) = 1.2214. Similarly, is β of x is equal to -0.1, we can interpret it as one unit increase in x decreases the probability of launch by 9.52%, given exp(-0.1) = 0.9048.

$$h(t|\mathbf{X}_{ijy}) = h_{i0}(t)\exp(patent_{ij}\beta_p + innovative_j\alpha_0 + patent_{ij}*innovative_j\alpha_1 + \mathbf{x}_{ijy}\boldsymbol{\beta}_x + \eta_{ATC1} + \mu_y + u_{ijy}) \quad (1)$$

We construct the launch data set for regressions based on launched molecule-market combinations by the following steps. Firstly, we define launch date of each pharmaceutical in each market conditional on the availability of the launch date. In the case where the exact launch date is unavailable but there is a launch record[35], we code the launch date as missing. Secondly, we construct a data set consisting of observations of all launch opportunities (i.e., all possible market-molecule combinations), where some of them have specified launch date, some of them have unspecified launch date which are recoded as missing, and the remaining market-molecule combinations have no occurrence of launch. Thirdly, we construct a larger data set containing annual observations of each market-molecule combination. The starting year of each market-molecule-year observation is the year of global launch of the product, and the last year of the market-molecule-year observation is either the local launch year if the product has been launched by the end of 2017 or 2017 if the product has not been launched in the market by the end of 2017. Market-molecule combinations with missing local launch date are dropped at this stage. The launch outcome indicator is coded as one only for the market-molecule-year combinations where the local launch of the product actually happens in the year. Otherwise, the launch outcome indicator is always coded as zero. Lastly, we merge other time varying variables such as demographic features and disease burden to the launch data set.

In the launch equation, we use the availability of product patent protection as the patent indicator instead of the actual patent status of each product in each market. The patent indicator is equal to one if the product patent application in pharmaceuticals could be filed ten years before the global launch of the product, which varies by market and by product. As stated before, we use ten years as the average lag from the date of patent filing in the market even though it may well take longer in some markets. In the price study, we have the data of protection date by molecule and by market. However, we do not use it in the launch study because firstly we are interested in the impact of regime change. Also, to examine the impact of patent protection, we must have a pharmaceutical patent data set where some market-molecule combinations are protected while others are not. In the protection data set, all molecules are protected in the 59 local markets for which we have data, and thus we are unable to have variation of patent status.

It is noteworthy that we aim to examine the overall impact of the introduction of product patents in pharmaceuticals on the probability of launch. We take the earliest appearance of a molecule as first launch, irrespective of being launched by the originator, the originator's licensee, or by generic firms. Since patent protection can effectively block generic entry and make the market potentially more profitable for originators, our estimated effect of patentability on launch is pooled across the two counteractive effects, i.e., the effect on originator launch likelihood and that on generic launch likelihood. The overall effect of patent may also vary across markets, depending on to which degree the markets rely on generics before adopting product patents, whether originators are willing to file the patent application in the local patent office, and local enforcement of patent protection, which are potential sources of endogeneity in this study. In addition, price control policy is another critical factor which determines the timing of launching new pharmaceuticals. However, we do not introduce them into our empirical study since no data on these policies have been collected systematically for the 70 independent markets in our sample.

5.2 Results of launch study

Table 6 presents baseline regression results of the launch study. We start from the interpretation of the patent indicator. Column (1) is a reference regression where the patent indicator is equal to one

[35] In the case where the launch date is unspecified in the raw data from IQVIA, we code them as missing launch date, and they are dropped in survival estimations (Kaplan-Meier Survival Curve and Cox Model). In the case where price data of the product in local market is available but launch date is not available in the raw launch data from IQVIA, we code the launch date as missing.

if the market had adopted product patent five years before the global launch of a new pharmaceutical. The five-year lag is in general shorter than the time lapse from filing a patent to commercialization of a new medicine, and we expected to see that this patent indicator has little impact on launch likelihood. As expected, patentability with five-year lag is insignificant in column (1). From column (2) to column (4), we use patentability with a ten-year lag. In column (2), without taking innovativeness of pharmaceuticals into account, patentability is positively significant. The introduction of product patents (with a ten-year lag) increases launch probability of new medicines by 10.5% compared to the market without product patent. In Column (3), we include one dummy of pharmaceutical innovativeness based on the classification in Lanthier et al. (2013) explained earlier. Compared to non-innovative medicines, innovative medicines are more likely to be launched by 16.9%. We introduce the interaction term between patentability and innovativeness in column (4), which is shown to be positively significant, but the significance of patentability itself disappears. In other words, when we allow patentability to have differentiated effects on launch probabilities of innovative and non-innovative medicines, we find that patentability can only facilitate diffusion of innovative pharmaceuticals and it has no effects on the launch likelihood of non-innovative medicines. We then focus on results of other variables. Log population is significantly negative, and since we use market fixed effects in the specification, we interpret this to mean that rich markets are highly attractive to pharmaceutical firms despite having declining population growth. GDP growth is also positively associated with launch probability. Increasing income by one percent leads to increases in launch likelihood by 0.26%. Disease burden, life expectancy, and health expenditure are also significant in some cases, but their magnitudes are very small.

In Table 7, we perform analyses by disease category. Explanatory variables in Table 7 are same as those in Table 6 column (4). Column (1) only contains pharmaceuticals used to treat non-communicable conditions[36] and column (2) contains the rest used to treat infectious conditions including HIV, malaria, and Tuberculosis (TB). In column (1), both patentability and the interaction term are positively significant, suggesting that the availability of the product patents in pharmaceuticals facilitates launches of pharmaceuticals for non-communicable conditions in general, although it works better for innovative medicines. The coefficient of innovativeness is insignificant, so that if we do not consider patents regime change, for medicines targeted at non-communicable conditions, products differing in innovativeness have the same probability of launch. We present results for medicines used to treat communicable conditions in column (2), where innovativeness is an important factor to accelerate launch. However, patentability is negatively significant, which means that the introduction of product patents delays launches of non-innovative products. For innovative medicines, the marginal effect of patentability is insignificant. The interpretation of this finding could be that the demand of medicines to treat infectious diseases is concentrated in relatively low income markets which used to rely much more on generics to meet local healthcare needs, and after product protection is introduced, the availability of new medicines may get worse because originators are not interested in these markets and generics are no longer able to enter the markets early. Also, originators are less motivated to launch non-innovative products, since these markets are likely to already have similar medicines. As a result, the availability of non-innovative medicines to treat infectious diseases is significantly worse off after the adoption of product patents regime. Results for HIV/AIDS, malaria and TB medicines and neoplasm medicines are presented in column (3) and (4) respectively. In column (3), HIV/AIDS medicines dominate this subgroup, where the interaction term between patentability and innovativeness is negatively significant. Patentability does facilitate global diffusion of HIV/AIDS, malaria and TB medicines, but only for non-innovative ones, probably because those innovative medicines for epidemics can be procured and launched in these markets in response to public health needs with donor money irrespective of their product patents regime. We also find that innovativeness is associated with faster launches, though this effect differs by patentability. Column (4) contains medicines to treat neoplasms (including malignant neoplasms and other neoplasms). Income growth is the only variable significant at five percent significance level, and the neither patentability nor innovativeness matter for the launch speed for such medicines, probably because anti-neoplastic medicines are in general difficult to copy and originators do not worry about generic competition.

Analyses by income group are shown in Table 8. Since launches in our sample took place from 1980 to 2017, we take income classification in 2000 as roughly being in the middle of this period. For high-income markets, the adoption of product patents increases launch likelihood by 29.7%.

[36] Non-communicable conditions include nutrition deficiency. In our sample, the two pharmaceuticals for nutritional condition are used to treat obesity.

Launches of innovative medicines are more likely to take place than non-innovative medicines by 37.7%. The interaction term is insignificant, showing that effects of patent do not discriminate by innovativeness. In column (2), patentability is not significant while the interaction term is positively significant, which shows that in middle-income markets, introducing product patents can facilitate launches of innovative medicines but non-innovative medicines are not affected by changes in patents regime. Noticeably, when we only consider the effect of the availability of product patents on innovative medicines, the marginal effect of this variable in middle-income markets is still smaller than that in high-income markets (i.e., 0.119 < 0.260). Column (3) presents result for low-income markets, where neither patentability nor the interaction term is significant, and therefore the adoption of product patents in pharmaceuticals makes no difference to the speed of launch. One explanation could be that patients in low-income markets are unable to afford most new medicines, and thus those markets are not attractive to pharmaceutical firms even if patent protection is available. Another reason could be that the introduction of product patents increases the launch likelihood of originator products but reduces that of generics in low-income markets. As a result, these two effects offset each other, and the overall effect of the change in patent regime is insignificant. For other variables, income growth is associated with faster launches, but this finding only holds for middle-income and low-income markets. Population growth is still negatively related to launch likelihood. For low-income markets, a one-year increase in life expectancy increases launch probability by 18.2%, suggesting that general improvement of health status leads to better availability of new medicines. We also perform regressions on samples of middle-income markets excluding China and low-income markets excluding India, which are shown in column (4) and (5). Findings still hold after excluding these two major markets in their respective income groups.

To sum up, we find that the introduction of product patents in pharmaceuticals increases launch likelihood by 10.5% on average, and this effect is concentrated on innovative medicines. Also, the launch likelihood of medicines used to treat different diseases is affected by the patent regime differently. For example, the launch speed of anti-neoplastic medicines is not subject to change in the patent regime at all, while innovative medicines used to treat other non-communicable conditions are sensitive to the adoption of product patents. Besides, the impact of changes in the patent regime vary by market, which results in faster launches in high-income markets but has no overall effect in low-income markets. For middle-income markets, the availability of a product patents regime selectively promotes launches of innovative medicines. In addition, innovative medicines are more likely to be launched, and the impact of innovativeness on launch probability is larger in markets where product patents are available. Lastly, in middle-income and low-income markets, increase in GDP per capita facilitates local launches, but population growth has negative effects on launch likelihood. This seems to indicate that income is the correct proxy for demand and not population per se. We also study the impact of DALY on launch likelihood, but in general, the effect is very little except for HIV/AIDS, malaria, and TB medicines.

6 PRICE STUDY

6.1 Specification of price study

In the price study, we focus on differential pricing across markets and examine if prices of originator and generic pharmaceuticals are adjusted to local income level. To this end, we analyse price variation between markets for each molecule. Unlike in the launch study, patent status here is controlled as one explanatory variable which affects pricing but is no longer the key variable of interest. The baseline specification is shown in Eq(2), where i indexes market, j indexes molecule, and y indexes year. Price data by molecule is available from 2007 to 2017. **x** includes socioeconomic variables and disease burden. **z** consists of two competition indicators, viz., the number of brands by molecule and the number of brands by ATC4. Both of them are in log form. Retail is a dummy which is equal to one if sales data was collected only from the retail sector in the market. Fixed effects at molecule-year level are introduced, so that we only consider variation between markets for each molecule in each year. We do not use market fixed effects, because it would wipe out variation between markets. Regressions on prices are performed by originator and generic products separately in order to learn about pricing strategies for these two groups of firms. In the case where pharmaceutical prices are fully differentiated according to income, the coefficient of log(GDP per capita) would be one, suggesting that drug prices increase proportionally with GDP per capita growth and patients in different markets spend the same proportion of their income on pharmaceuticals. A zero coefficient of log(GDP per capita) means that there is no differential pricing at all and that local income is not a factor determining pharmaceutical prices.

$$Log(P_{ijy}) = \mathbf{x}_{ijy}\boldsymbol{\beta} + \mathbf{z}_{ijy}\,\boldsymbol{\gamma} + Retail_i\,\pi + \lambda_{jy} + u_{ijy} \quad (2)$$

In the baseline Eq(2), the patent indicator is omitted for two reasons. Firstly, as patent status affects prices by eliminating competitors, it is supposed to have no direct impact on price conditional on the number of brands by molecule. Secondly, the patent protection dates are only available for a limited range of molecules[37] in 59 markets where patent status of each molecule is either active or expired. Sample selection issues may arise once we apply this indicator. We incorporate market protection expiry related variables in Eq(3) to examine price differentiation in markets where the protection is either active or expired. Only observations with available protection data are used here. Expiry is coded as one if protection of molecule j in market i has expired in year y. Interaction terms of expiry and each of the competition indicators are also included in Eq(3).

$$Log(P_{ijy}) = Expiry_{ijy}\varphi_0 + Expiry_{ijy}*\mathbf{z}_{ijy}\,\boldsymbol{\varphi} + \mathbf{x}_{ijy}\boldsymbol{\beta} + \mathbf{z}_{ijy}\boldsymbol{\gamma} + Retail_i\pi + \lambda_{jy} + u_{ijy} \quad (3)$$

6.2 Results of price study

In Table 9, we present regressions on prices of originator products with protection expiry variable as specified in Eq(3). To use this variable, almost half of price observations have to be dropped due to missing values.[38] Column (1) is the regression for all available originator prices. Column (2) and (3) are regressions by innovativeness. From column (4) onwards, we present regressions by disease category. Firstly, we find that the expiry dummy is negatively significant, except in the last two columns. In other words, holding other variables constant, originator prices decline after expiry of the protection. Secondly, we find competition both within the molecule and within ATC4 can effectively drive prices down, either before or after the protection expires. The effects of within-molecule competition are clearly greater after the end of protection.[39] Conversely, brand competition within ATC4 is effective before the end of protection. In column (1), increases in the number of brands within the molecule by one percent after expiry of the protection leads to decrease in originator price by 0.101%, which is five times the effect (-0.022) before expiry. For socio-economic variables, population, income and health expenditure are positively significant, suggesting that prices of originator products are higher in larger and richer markets. DALY is negatively significant, so that conditional on population and income, prices also decline as local disease burden increases presumably because of higher volumes. Life expectancy is significant, but the magnitude is trivial. Prices only collected in the retail sector are higher than those collected from combined sectors or hospital sector by 7.9%. In terms of differential pricing, the coefficient of GDP per capita is 0.024 in column (1), which suggests that one percent growth in income leads to increases in pharmaceutical prices by 0.024%. Across all columns, coefficient of GDP per capita ranges from being insignificant to 0.127, and we find a stronger differential pricing of originator products for innovative medicines and for medicines used to treat infectious conditions. Though some values are positive, the magnitude of this coefficient is very low and far from being adjusted to local income level.

We describe the sample selection issue in Table 9 and the reason why we drop expiry variable in further regressions in this paragraph. Table 10 presents results using the same data set (i.e., only observations with protection data) as in Table 9 but without the expiry variable as specified in Eq(2). All findings of competition and socio-economic variables still hold in Table 10 without changing much in coefficients, suggesting that once competition intensity is controlled, we no longer need to control the protection status directly. The coefficient of GDP per capita changes from 0.024 in column (1) Table 9 to 0.027 in column (1) Table 10. We agree that dropping the expiry dummy could introduce bias in our estimation since the dummy itself is significant in Table 9. However, given the minor differences between coefficients of GDP per capita in Table 9 and Table 10, we conclude that excluding the expiry variable could only cause very limited bias on the study of differential pricing.

[37] We matched protection data of 481 molecules out of 578 molecules, but the number of molecules with protection information is different by market. 16 molecules out of the 481 are dropped in regression due to no DALY to link.

[38] Among 186837 price observations, there are 95515 observations having matched protection data.

[39] Based on the originator price data set with available protection variable (95515 observations), there are 1.82 brands on average in the molecule market before the end of protection. Also, before the expiration, more than 75 percent molecule-market-year combinations have single brand. In theory, there should be no other brands other than originator ones before the end of product patent protection. However, there are observations having more than one brand before protection expires in our sample, probably because "protection" in the IQVIA database does not necessarily mean "product patent protection" or "market exclusivity". Also, these protection dates are estimated, so they may be inaccurate.

Thus, we perform regressions on originator prices with all price observations without the expiry indicator and present results in Table 11. In Table 11 column (1), we find that the coefficient of GDP per capita is 0.110 for all pharmaceuticals, which is much larger than the corresponding values in Table 9 and Table 10. Since the specifications of Table 10 and Table 11 are identical and the only difference is the data sets used, we conclude that using the price data set consisting of observations with available protection status data leads to sample selection issues, which tends to underestimate differential pricing. There are only 59 markets in the protection data set which covers most high-income and upper-middle income markets but excludes low-income markets such as Bangladesh and French West Africa, so that income variation between markets is limited and the effect of income on price cannot be fully captured. We drop the expiry variable in further regressions because we are interested in the effects of income and we also have within molecule and within ATC4 controls on competition.

Our analyses on originator prices are based on regressions in Table 11. Effects of GDP per capita do not vary much by innovativeness. In terms of disease category, differential pricing is stronger for medicines to treat infections than non-communicable conditions. In column (6) and (7), we present two more regressions specifically for HIV, Malaria, and TB medicines and for neoplasm medicines. The former group of medicines is dominated by HIV/AIDS medicines. We find that prices of originator HIV type medicines are more sensitive to local income level compared to other medicines, while prices adjustment to income is weaker than average for neoplasm medicines. All those findings still hold when we compare standardized coefficients of log(GDP per capita) cross columns. Increases in log(GDP per capita) by one standard deviation leads to increases in log(originator prices) of HIV, Malaria and TB medicines by 0.093 standard deviation. For other medicines, increases in log-income have smaller effects on their originator prices. Apart from income levels, we also see the effect of income distribution on originator pricing. Gini coefficient is significant in most columns, suggesting that pharmaceutical firms are inclined to set a high price and target the very rich population in markets where income is distributed unequally (as predicted by Flynn et al. 2009). On average, increasing Gini coefficient by one percent leads to increase in price by 0.587%. Prices of HIV type medicines are negatively correlated to inequality, probably because prices of these medicines are influenced by special policies decided by donors. For other variables, we do not repeat their interpretation here since coefficients do not change much compared to Table 9.

Table 12 presents regressions on prices of generics using the specification in Eq(2). Since exclusivity of originators no longer holds once generics appear in the molecule market, we do not consider any protection variable in the study of generic prices. In Table 12, we find that factors determining prices of originator pharmaceuticals also affect generic pricing, and to an even greater extent. To start with, brand competition within the molecule market can effectively reduce generic prices. Increasing the number of brands by one percent contributes to price decline by 0.147%, which is much higher than the effect on originator products. While the count of brands by ATC4 class is negatively associated with originator prices, it may result in higher generic prices of infectious diseases' medicines and neoplasm medicines – we interpret this to mean that ATC4 level competition is not effective to drive prices down for generics. Secondly, differential pricing is stronger for generic products either measured in original (non-standardized) coefficients or in standardized coefficients, which also varies by innovativeness and by disease category. For innovative generics, one percent GDP per capita increase leads to increase in generic price by 0.316%, while for non-innovative medicines, this magnitude is 0.203%. Again, differential pricing is stronger for infectious disease medicines, especially for HIV type medicines. In column (6), the coefficient of income for HIV type medicines is 0.686, implying that generic prices are adjusted by two thirds to income differentials across markets. In terms of standardized coefficients, increasing log(GDP per capita) by one standard deviation leads to increasing in log(generic price) by around 0.084 standard deviation for all products, but this value for generic medicines used to treat infectious diseases is much higher. Measured in standardized coefficients, generic prices of HIV, Malaria, and TB medicines are also better adjusted to local income among generics, seeing that increasing log(GDP per capita) by one standard deviation corresponds to increasing in log(generic price) by one half standard deviation.

For the remaining variables in Table 12, signs of coefficients are similar to that shown in Table 11 on regressed originator prices. Generics are more expensive in markets where population is large and income is distributed unequally. Compared to originators, generic firms are much more sensitive to local income distribution. Conditional on population, disease burden is negatively correlated to generic price probably due to the trade-off between price and volume. Life expectancy and health expenditure are indicators of the quality of public health system and national investment in health,

which in general link to higher pharmaceutical prices. In column (5), an increase in life expectancy by a year contributes to decrease in prices of infection generics by 2.2%. One explanation could be that a longer life expectancy is the result of eliminating some parasitic and infectious conditions which used to be fatal, so that the demand for infectious disease medicines is smaller in markets where people live long. As a result, prolonged life expectancy is associated with lower price of infectious disease medicines.

In this study, the substitutes of each product are defined as products within the same ATC4 group. However, we notice that some studies use a higher aggregated level – ATC 3 to classify molecules instead of ATC4, which suggests that molecules within the same ATC3 class may also substitute each other to some extent (Danzon et al., 2005; Kyle and Qian, 2014). We replicate regressions in Table 11 and Table 12 using the count of brands per ATC3 rather than per ATC4 as a robustness check. We present results in Table 13 and Table 14, and all previous findings on differential pricing and competition still hold. In Table 13, coefficients of the count of brands by ATC3 are smaller in absolute value than that by ATC4 in Table 11, showing that brand competition within ATC4 group is more effective to drive down originator prices compared to that within ATC4 group.

In conclusion, we do find evidence for differential pricing by income for both originator and generic products. Overall, originators differentiate prices by about 11% and generics by about 26%. However, pharmaceutical prices are far from being fully adjusted to local income level in either case. For both originator and generic products, prices of HIV type medicines are better adjusted to local income, and differential pricing is larger for pharmaceuticals used to treat infectious diseases than those to treat non-communicable conditions. Compared to originator products, pricing of generics is more sensitive to properties of the pharmaceutical (e.g. innovativeness and disease category), local income level, as well as income distribution. We also find that competition can effectively drive down prices in both originator and generic pricing, especially the within-molecule competition. This shows that in the absence of market exclusivity, prices are much lower after competitor's entry.

7 ROBUSTNESS CHECKS AND DISCUSSION ON ENDOGENEITY

We perform other specifications and discuss potential endogeneity issues in this section. We conduct further regressions using our launch data to check robustness of our specification, including parametric proportional hazard model specification, regressions with Market*ATC1 fixed effects, and adding interaction terms in regressions. These regressions are presented below, and our baseline findings in the launch study are robust to these checks. However, our launch study and price study may still be subject to endogeneity problems. Hence, we discuss these issues in this section.

In the launch study, we use semi-parametric model to estimate the impacts of patentability on launch hazard without specifying the distribution of the hazard function. Since a parametric model is supposed to be more efficient if the model is specified correctly, we perform regressions with parametric proportional hazard model in Table 15 column (2) and column (3). Compared to the baseline result given by Cox model in column (1), the parametric model with Gompertz distribution produces extremely similar estimates in terms of coefficients and standard errors, while coefficients of patentability and innovativeness given by Weibull model are much larger. We conclude that the hazard function follows Gompertz distribution based on the strong similarity of estimates produced by Cox semi-parametric model and Gompertz model.[40] We also find that parametric estimation does not provide much gain in efficiency in our case, because standard errors do not vary much from column (1) to column (3).

Apart from efficiency issues, our study may also be subject to omitted variable problems. For example, we do not control for price regulation policies in each market, which can affect both launch likelihood and drug prices. In the launch study, market fixed effects and ATC1 fixed effects are applied separately. Considering unobservable factors which affect launch likelihood differently by market and by the type of medicines (e.g., in each market, price controls are set differently according to the disease category of medicines), we conduct robustness checks with Market*ATC1 fixed effects by Cox model and present results in column (4) Table 5. After controlling for unobservable

[40] "When you engage in this kind of parametric estimation, it is prudent to compare the estimated coefficients with those from a Cox model fit to verify that they are roughly similar. If they prove not to be similar, then this is evidence of a misparameterized underlying baseline hazard." See Cleves et al.(2008), page 234.

heterogeneity by market*ATC1, we find result does not change from the baseline. We also apply Market*ATC1 fixed effects to subsamples by income level in 2000, and findings in column (5) (6) (7) are highly consistent with Table 8.

In the launch study, our baseline result (Table 6 column 4) shows that impacts of the change in patents regime differ by innovativeness of medicines. However, we assume that marginal effects on launch hazard of other socioeconomic variables do not vary by innovativeness of medicines. If they do, our specification will have omitted variable problems. We relax this assumption by adding interaction terms of innovativeness and each socioeconomic variable. Regression results with interaction terms of innovativeness are presented in Table 16. From column (1) to column (5), we use Cox model. Column (6) is estimated by Gompertz model. After including interaction terms of innovativeness and all other variables, we find patentability turns to significant but innovativeness per se loses its significance in column (2). Gompertz model in column (6) provides a very similar result to column (1), though innovativeness is significant at ten percent significance level. The interaction terms of population, GDP per capita, and health expenditure per GDP are positively significant, showing that compared to non-innovative ones, innovative medicines are more likely to be launched in markets of high population growth, high income, and high healthcare expenditure. The interaction term of DALY is negatively significant, implying that innovative medicines are less likely to be available soon in markets of high disease burden. The reason of this finding could be markets with high disease incidences may accelerate approvals of non-innovative medicines seeing that the effectiveness of me-too drugs has been proven in their markets. However, for innovative products, those markets of high disease burden may wait to see if they are really effective in other markets. We preform regressions with interaction terms by income from column (3) to column (5). Again, as shown in Table 8, we find introducing product patents can facilitate launches of all new medicines in high-income market, only innovative medicines in middle-income markets, and none in low-income markets. We also notice that innovative medicines are more likely to be launch in middle-income markets, no matter whether product patents are available or not in the local market. For high-income markets, the introduction of product patents is particularly important for drug launches. New pharmaceuticals are more likely to be launched in patentable high-income markets by 35.4% (i.e., exp(0.303) – 1 = 0.354) compared to non-patentable ones. For middle-income markets, launch likelihood of a new pharmaceutical depends largely on innovativeness of the medicine, patentability, and income growth. The launch likelihood of an innovative medicine in middle-income markets is twice higher (i.e., exp(1.127) – 1 = 2.09) than that of non-innovative medicines. For low-income markets, if not none, changes in patents regimes have limited impact on the availability of new pharmaceuticals.

We discuss sources of potential endogeneity in this paragraph. First, we do not take firm level factors into account in our study. The firm size, market power, and local experiences of pharmaceutical firms (e.g., headquarter location, the number of products launched in local market, revenue from the market) may affect the launch delay and the price of new products in the local market. Kyle (2007) finds that new drugs are more likely to be launched in markets which share a border or a language of a drug firm's country of headquarters and in markets where the originator has more experience. In this paper, we omit firm level factors, because it is difficult to track the ownership of each molecule. Marketing rights of pharmaceuticals can be transferred between firms over time, and merger and acquisition activities are common in pharmaceutical industry. We tried to consult IQVIA for firm level data, but we could not figure out the exact firm to link for each molecule-market-year combination.[41] Since firm characteristics are possibly correlated with local policy regimes and income level, missing firm data may cause biased estimation in both launch and price study. Second, we assume exogenous introduction of product patents in pharmaceuticals in the launch study and attribute this policy change to the obligation under TRIPS.[42] However, the adoption of product patents in pharmaceuticals may depend on other unobservable factors which also determine the launch likelihood. For example, pharmaceuticals become patentable in a market, because pharmaceutical firms find this market profitable and lobby government to strengthen protection of intellectual property. In this case, the impact of patentability would be overestimated. Third, as aforementioned, our study does not consider price control policy due to data unavailability, though price control has direct impacts on launch delay and drug prices. The stringency of price control can vary by medicines in each market. We try to eliminate effects of price control in the launch study by

[41] For example, a new medicine x is developed by firm A, and firm A is acquired by firm B afterwards. Firm B is a subsidiary of firm C. Marketing rights of x also belong to different firms by market. In this case, we do not know information of which firm should be linked to x.

[42] Since we have market fixed effects, we only consider changes in patentability in one market instead of patentability status per se.

introducing market*ATC1 fixed effects in Table 15. However, we cannot apply market fixed effects to regressions on prices given our research interests in differential pricing. As a result, the price study is more likely to be subject to biased estimation caused by missing price control variable.

8 CONCLUDING REMARKS

Our paper is different from past work we have cited in that we differentiate between innovative pharmaceuticals and non-innovative ones; we analyse our research questions according to different disease conditions, as well as income levels of groups of countries; and for the price study, we differentiate between the pricing strategies of originator and those of generic companies.

In the launch study, we find introducing product patent protection has a positive effect on launch likelihood, especially for innovative pharmaceuticals, but this effect is limited in low-income markets – perhaps because they relied more on generics during much of our study period, possible due to non-availability of product patent protection. The launch of non-innovative pharmaceuticals seems to be facilitated by the patent regime only in high income markets. Innovative pharmaceuticals are launched sooner than non-innovative ones with or without patent protection in non-low-income markets. The effects of patentability on the launch likelihood also vary by disease category of medicines. The diffusion of medicines used to treat non-communicable conditions is facilitated by patentability on average, though the availability of anti-neoplastic medicines is not subject to changes in patents regime.

In the price study, examining recent IQVIA data from 2007 to 2017, we find evidence of differential pricing for both originator and generic products. Overall, originators differentiate by about 11% and generics by about 26%. Differential pricing is larger for pharmaceuticals to treat infectious diseases, particularly for HIV/AIDs medicines, than for non-communicable diseases. However, pharmaceutical prices are far from being fully adjusted to local income levels in either case. Compared to originator products, pricing of generics is more sensitive to whether the medicine is an innovative one or not, disease condition, local income level, as well as income distribution. The study also finds that competition, especially the within-molecule competition, can effectively drive down prices in both originator and generic markets.

REFERENCES

Cleves, M., Gould, W., Gutierrez, R., & Marchenko, Y. (2008). An introduction to survival analysis using Stata. Stata press.

Chaudhuri, S., Goldberg, P. K., & Jia, P. (2006). Estimating the effects of global patent protection in pharmaceuticals: a case study of quinolones in India. American Economic Review, 96(5), 1477-1514.

Cockburn, I. M., Lanjouw, J. O., & Schankerman, M. (2016). Patents and the global diffusion of new drugs. American Economic Review, 106(1), 136-64.

Congress, U. S. (1993). Office of Technology Assessment, 1993. Pharmaceutical R&D: Costs, Risks, and Rewards. Washington, DC: US Government Printing Office.

Costa-Font, J., McGuire, A., & Varol, N. (2015). Regulation effects on the adoption of new medicines. Empirical Economics, 49(3), 1101-1121.

Danzon, P. M., Wang, Y. R., & Wang, L. (2005). The impact of price regulation on the launch delay of new drugs—evidence from twenty-five major markets in the 1990s. Health Economics, 14(3), 269-292.

Danzon, P. M., & Furukawa, M. F. (2008). International prices and availability of pharmaceuticals in 2005. Health Affairs, 27(1), 221-233.

Danzon, P. M., Mulcahy, A. W., & Towse, A. K. (2015). Pharmaceutical pricing in emerging markets: effects of income, competition, and procurement. Health Economics, 24(2), 238-252.

Delgado, M., Kyle, M., & McGahan, A. M. (2013). Intellectual property protection and the geography of trade. The Journal of Industrial Economics, 61(3), 733-762.

DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: new estimates of R&D costs. Journal of health economics, 47, 20-33.

Duggan, M., Garthwaite, C., & Goyal, A. (2016). The market impacts of pharmaceutical product patents in developing countries: Evidence from India. American Economic Review, 106(1), 99-135.

European Commission, Competition, D. G. (2009). Pharmaceutical sector inquiry final report.

Flynn, S., Hollis, A., & Palmedo, M. (2009). An economic justification for open access to essential medicine patents in developing countries. The Journal of Law, Medicine & Ethics, 37(2), 184-208.

Grabowski, H. G., & Kyle, M. (2007). Generic competition and market exclusivity periods in pharmaceuticals. Managerial and Decision Economics, 28(4-5), 491-502.

Kremer, M. (2002). Pharmaceuticals and the developing world. Journal of Economic Perspectives, 16(4), 67-90.

Kyle, M. K. (2006). The role of firm characteristics in pharmaceutical product launches. The RAND Journal of Economics, 37(3), 602-618.

Kyle, M. K. (2007). Pharmaceutical price controls and entry strategies. The Review of Economics and Statistics, 89(1), 88-99.

Kyle, M. K., & McGahan, A. M. (2012). Investments in pharmaceuticals before and after TRIPS. Review of Economics and Statistics, 94(4), 1157-1172.

Kyle, M., & Qian, Y. (2014). Intellectual property rights and access to innovation: evidence from TRIPS (No. w20799). National Bureau of Economic Research.

Lanjouw, J. O. (2005). Patents, price controls and access to new drugs: how policy affects global market entry (No. w11321). Cambridge (MA): National Bureau of Economic Research.

Lanthier, M., Miller, K. L., Nardinelli, C., & Woodcock, J. (2013). An improved approach to measuring drug innovation finds steady rates of first-in-class pharmaceuticals, 1987–2011. Health Affairs, 32(8), 1433-1439.

Liu, M., & La Croix, S. (2015). A cross-country index of intellectual property rights in pharmaceutical inventions. Research Policy, 44(1), 206-216.

Lopez, A. (2009). Innovation And Appropriability. Empirical Evidence And Research Agenda, WIPO International.

Mestre-Ferrandiz, J., Sussex, J., & Towse, A. (2012). The R&D cost of a new medicine. London: Office of Health Economics

Park, W. G. (2008). International patent protection: 1960–2005. Research policy, 37(4), 761-766.

Rickwood, S. (2017). Prescription medicines trends: an overview and perspective on two therapy areas. Retrieved from https://www.who.int/phi/2-SarahRickwood.pdf

Sood, N., Shih, T., Van Nuys, K., & Goldman, D. (2017). Follow the money: the flow of funds in the pharmaceutical distribution system. Health Affairs Blog. June, 13.

Varol, N., Costa-Font, J., & McGuire, A. (2010). Do international launch strategies of pharmaceutical corporations respond to changes in the regulatory environment?. LSE Health Working paper, No. 19/2010

Varol, N., Costa-Font, J., & McGuire, A. (2012). Does adoption of pharmaceutical innovation respond to changes in the regulatory environment?. Applied Economic Perspectives and Policy, 34(3), 531-553.

Wagner, S., & Wakeman, S. (2016). What do patent-based measures tell us about product commercialization? Evidence from the pharmaceutical industry. Research Policy, 45(5), 1091-1102.

Watal, J. (2015). Patents: An Indian Perspective. In J. Watal. & A. Taubman.(Eds.), The Making of the TRIPS Agreement. (pp. 295-320). Geneva: World Trade Organization

World Intellectual Property Organization. (1988). Existence, scope and form of generally internationally accepted and applied standards/norms for the protection of intellectual property (Report No. MTN.GNG/NG11/W/24). Retrieved from https://www.wto.org/gatt_docs/English/SULPDF/92040090.pdf

Table 1. Distribution of 556 molecules by innovativeness and by disease category

Disease Category	innovative drugs	share in group	additional drugs	share in group	WHO GHE code
Tuberculosis (TB)	2	0.7%	0	0.0%	30
HIV/AIDS	22	7.2%	3	1.1%	100
Diarrheal diseases	2	0.7%	2	0.7%	110
Hepatitis	5	1.6%	3	1.1%	185
Malaria	2	0.7%	0	0.0%	220
Respiratory infections	6	2.0%	5	1.8%	380
Neglected tropical diseases	5	1.6%	0	0.0%	210 (excl. 220), 330
Other infectious diseases	15	4.9%	23	8.5%	40, 370
Nutritional deficiencies	2	0.7%	0	0.0%	540
Diabetes	8	2.6%	11	4.1%	800
Endocrine, blood, immune disorders	14	4.6%	8	3.0%	810
Mental and behavioural disorder	12	3.9%	24	8.9%	820
Neurological conditions	19	6.2%	20	7.4%	940
Sense organ diseases	19	6.2%	18	6.6%	1020
Cardiovascular diseases	33	10.7%	51	18.8%	1100
Respiratory diseases	6	2.0%	17	6.3%	1170
Digestive diseases	8	2.6%	10	3.7%	1210
Genitourinary diseases	3	1.0%	16	5.9%	1260
Skin diseases	10	3.3%	10	3.7%	1330
Musculoskeletal diseases	12	3.9%	13	4.8%	1340
Congenital anomalies	12	3.9%	0	0.0%	1400
Neoplasms	89	29.0%	22	8.1%	610, 790
other (anaesthetics, contraceptive means, or antidotes)	1	0.3%	15	5.5%	-
sum	307	100.0%	271	100.0%	-

Table 2: Summary statistics of variables

	(1)	(2)	(3)	(4)	(5)
VARIABLES	N	mean	s.d.	min	max
World Development Indicators 1980-2017					
Population (millions)	2,660	70.94	190.5	0.364	1,379
GDP per capita (1000 USD)	2,505	14.56	17.23	0.094	119.2
Gini Coefficient (%)	1,540	38.37	9.066	21	64.80
Life Expectancy	2,660	72.78	6.184	46.54	84.28
Health Expenses/GDP (%)	1,224	6.708	2.541	1.933	16.84
Disability Adjusted Life Year (1,000 years)					
DALY 2000	1,496	996.8	4,024	0.00	64,161
DALY 2010	1,496	1,022	4,144	0.00	81,459
DALY 2015	1,496	1,048	4,413	0.00	95,098
Originator prices equation					
Price (per kg or IU)	186,837	5.79E+07	3.99E+08	6.31E-07	5.38E+10
Expiry dummy	95,515	0.448	0.497	0	1
Brands by molecule	186,837	4.255	8.608	1	230
Brands by ATC4	186,837	30.32	58.12	1	2719
Brands by ATC3	186,837	41.58	72.00	1	3033
Generic price equation					
Price (per kg or IU)	89,740	8168597	2.43E+08	5.62E-08	5.83E+10
Expiry dummy	33,575	0.873	0.333	0	1
Brands by molecule	89,740	8.134	11.87	1	230
Brands by ATC4	89,740	49.95	85.46	1	2719
Brands by ATC3	89,740	66.89	112.4	1	3033

Notes: Summary statistics of the price study are calculated based on observations used in panel regressions. We take no account of observations in which the molecule was present in single market in the given year, and these observations are dropped after within transformation.

Table 3: Survival estimates of launches by patentability and by income level

	Time by which 25% launched (years)				Fraction launched within 10 years		
Income Group	patent	no patent	difference		patent	no patent	difference
Low Income	5.51	5.84	0.33		37.7%	39.7%	-2.1%
Middle Income	2.34	4.67	2.33		58.9%	43.9%	15.0%
High Income	1.25	2.67	1.42		68.3%	56.3%	12.0%

Notes: This analysis is based on Kaplan-Meier survival function estimates with launch outcomes of 38,538 molecule-market combinations for 556 molecules in 70 markets, including 24,730 launches.

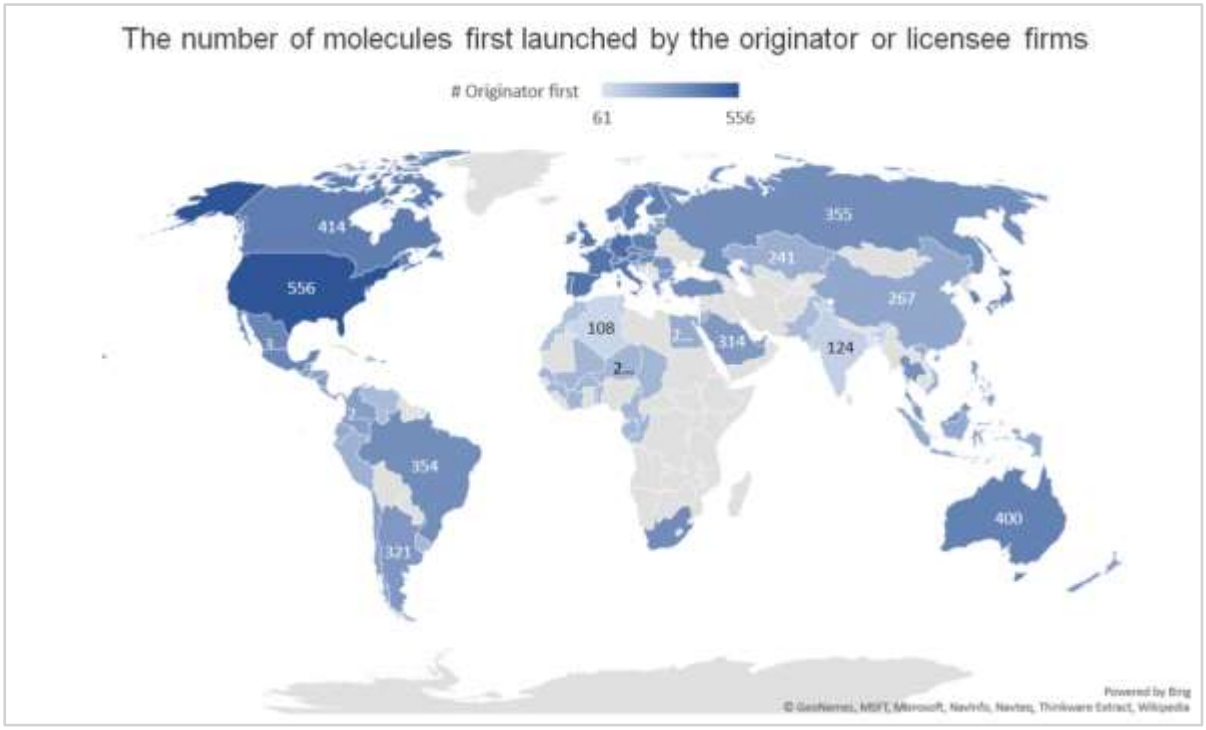

Figure 3a: The number of molecules first launched by the originator or licensee (among 556 molecules)

Notes: This graph is based on 22778 launches by originators or licensees. One special case is counted where TOPOTECAN has been launched in Saudi Arabia by both originator and generic firms, but launch date in neither form was specified in the raw data. We presume that the originator launched TOPOTECAN in Saudi Arabia prior to generic entry in this case.

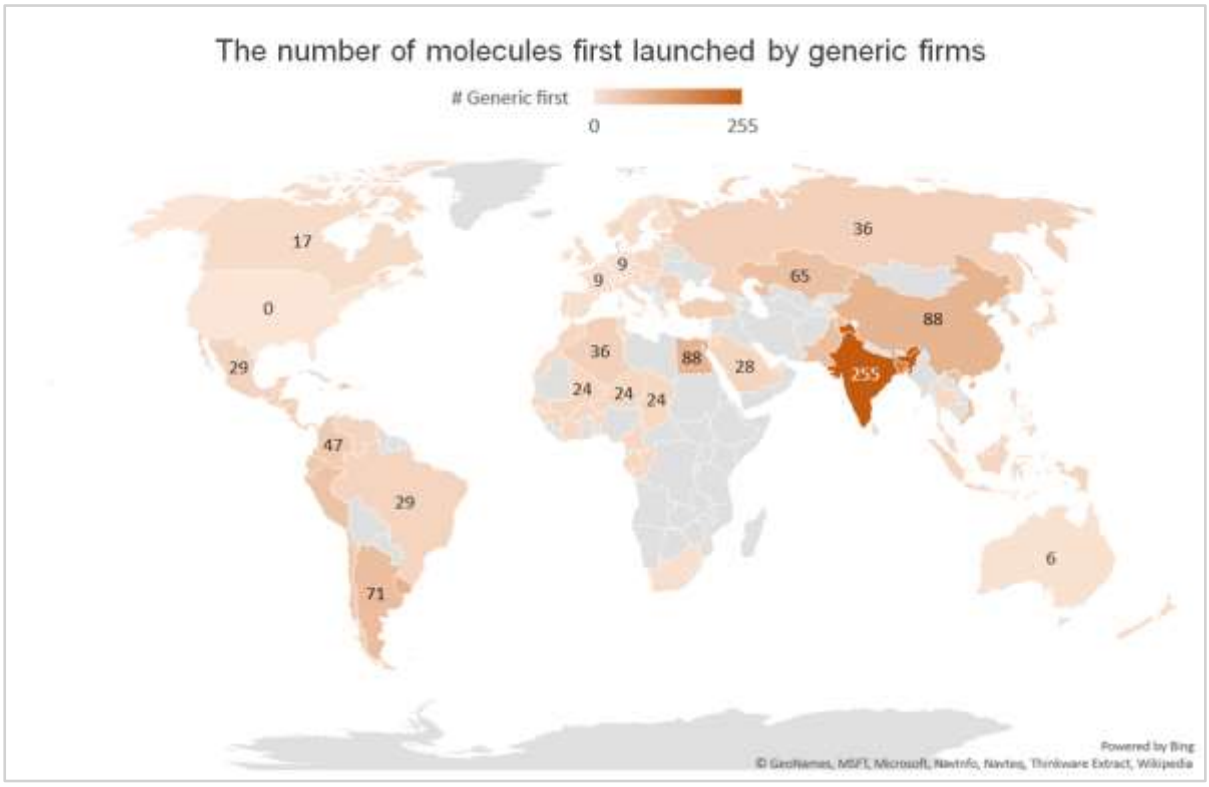

Figure 3b: The number of molecules first launched by generic firms (among 556 molecules)

Notes: This graph is based on 2334 launches by generic firms.

Map disclaimer: Maps are for graphical purposes only. The designations employed and the presentation of the materials on the maps do not imply the expression of any opinion whatsoever on the part of the WTO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Table 4a: Comparison of originator prices across markets in USD

Top 20 markets having the most among the highest-five-priced originator products (in USD)					Top 20 markets having the most among the lowest-five-priced originator products (in USD)				
No.	Market	Count of highest-five prices	Total available prices	Share of high prices	No.	Market	Count of lowest-five prices	Total available prices	Share of low prices
1	Puerto Rico	3297	3888	84.8%	1	Turkey	2354	3386	69.5%
2	US	3279	4442	73.8%	2	India	1017	1851	54.9%
3	Venezuela	986	1891	52.1%	3	Pakistan	1045	1992	52.5%
4	Colombia	1010	2549	39.6%	4	Bangladesh	369	781	47.2%
5	Japan	1056	3440	30.7%	5	Egypt	1108	2366	46.8%
6	Mexico	954	3453	27.6%	6	Korea	885	3573	24.8%
7	Dominican Rep	484	1883	25.7%	7	South Africa	731	3381	21.6%
8	Brazil	788	3242	24.3%	8	Hong Kong	655	3526	18.6%
9	Canada	812	3852	21.1%	9	Vietnam	373	2096	17.8%
10	Switzerland	758	4071	18.6%	10	Malaysia	553	3224	17.2%
11	Germany	773	4564	16.9%	11	Czech	589	3595	16.4%
12	Peru	317	1920	16.5%	12	UK	715	4433	16.1%
13	Australia	585	3786	15.5%	13	Romania	493	3068	16.1%
14	Chile	437	2830	15.4%	14	Argentina	441	2943	15.0%
15	Kazakhstan	275	1976	13.9%	15	Estonia	296	2152	13.8%
16	Russia	416	3451	12.1%	16	Ecuador	322	2364	13.6%
17	Uruguay	228	1913	11.9%	17	Russia	469	3451	13.6%
18	New Zealand	329	2797	11.8%	18	Greece	475	3546	13.4%
19	Philippines	308	2736	11.3%	19	Spain	582	4418	13.2%
20	Argentina	317	2943	10.8%	20	Italy	570	4363	13.1%

Table 4b: Comparison of originator prices across markets in price adjusted to GDP per capita

Top 20 markets having the most among the highest-five-priced originator products (adjusted price = price / GDP per capita)					Top 20 markets having the most among the lowest-five-priced originator products (adjusted price = price / GDP per capita)				
No.	Market	Count of highest-five prices	Total available prices	Share of high prices	No.	Market	Count of lowest-five prices	Total available prices	Share of low prices
1	Fr W Africa	1582	1741	90.9%	1	Luxembourg	2704	2839	95.2%
2	Philippines	2367	2736	86.5%	2	Norway	3569	4088	87.3%
3	Vietnam	1525	2096	72.8%	3	Switzerland	2501	4071	61.4%
4	Bangladesh	472	781	60.4%	4	Australia	1425	3786	37.6%
5	Pakistan	1167	1992	58.6%	5	Singapore	1142	3297	34.6%
6	Indonesia	1402	2429	57.7%	6	Ireland	1291	3946	32.7%
7	India	912	1851	49.3%	7	Sweden	1108	4112	26.9%
8	C America	1232	2688	45.8%	8	Belgium	881	4061	21.7%
9	Colombia	1038	2549	40.7%	9	UK	953	4433	21.5%
10	Morocco	547	1624	33.7%	10	Netherlands	450	2155	20.9%
11	Peru	553	1920	28.8%	11	Hong Kong	723	3526	20.5%
12	Puerto Rico	1110	3888	28.5%	12	Austria	683	4118	16.6%
13	Dominican Rep	499	1883	26.5%	13	Finland	623	3913	15.9%
14	Thailand	766	3244	23.6%	14	Germany	643	4564	14.1%
15	Bulgaria	617	2972	20.8%	15	New Zealand	378	2797	13.5%
16	Jordan	395	1957	20.2%	16	France	508	4325	11.7%
17	Mexico	589	3453	17.1%	17	Italy	493	4363	11.3%
18	China	430	2638	16.3%	18	Japan	368	3440	10.7%
19	South Africa	489	3381	14.5%	19	Kuwait	217	2085	10.4%
20	Brazil	444	3242	13.7%	20	Korea	364	3573	10.2%

Table 5a: Comparison of generic prices across markets in USD

Top 20 markets having the most among the highest-five-priced generic products (in USD)					Top 20 markets having the most among the lowest-five-priced generic products (in USD)				
No.	Market	Count of highest-five prices	Total available prices	Share of high prices	No.	Market	Count of lowest-five prices	Total available prices	Share of low prices
1	Venezuela	684	1186	57.7%	1	Bangladesh	1035	1664	62.2%
2	Puerto Rico	978	1841	53.1%	2	India	1390	2239	62.1%
3	Brazil	591	1566	37.7%	3	Pakistan	777	1549	50.2%
4	Mexico	554	1488	37.2%	4	New Zealand	466	1020	45.7%
5	Colombia	561	1571	35.7%	5	Egypt	729	1736	42.0%
6	Japan	342	1034	33.1%	6	Turkey	542	1552	34.9%
7	US	578	1873	30.9%	7	Netherlands	338	1025	33.0%
8	Peru	440	1443	30.5%	8	Uruguay	478	1811	26.4%
9	Philippines	317	1191	26.6%	9	Hong Kong	258	1059	24.4%
10	Dominican Rep	370	1409	26.3%	10	Vietnam	386	1658	23.3%
11	UAE	155	611	25.4%	11	Sweden	285	1279	22.3%
12	Ireland	268	1113	24.1%	12	Singapore	172	787	21.9%
13	Canada	380	1597	23.8%	13	Malaysia	233	1169	19.9%
14	Chile	346	1506	23.0%	14	China	374	2036	18.4%
15	Switzerland	266	1196	22.2%	15	US	331	1873	17.7%
16	Australia	280	1263	22.2%	16	UK	290	1705	17.0%
17	Indonesia	260	1184	22.0%	17	Poland	244	1582	15.4%
18	Argentina	387	1795	21.6%	18	Norway	156	1183	13.2%
19	Kuwait	92	430	21.4%	19	Germany	232	1784	13.0%
20	UK	347	1705	20.4%	20	Portugal	182	1508	12.1%

Table 5b: Comparison of generic prices across markets in price adjusted to GDP per capita

Top 20 markets having the most among the highest-five-priced generic products (in adjusted price = price / GDP per capita)					Top 20 markets having the most among the lowest-five-priced generic products (in adjusted price = price / GDP per capita)				
No.	Market	Count of highest-five prices	Total available prices	Share of high prices	No.	Market	Count of lowest-five prices	Total available prices	Share of low prices
1	Fr W Africa	737	822	89.7%	1	Norway	920	1183	77.8%
2	Philippines	1045	1191	87.7%	2	Luxembourg	484	725	66.8%
3	Indonesia	706	1184	59.6%	3	Netherlands	587	1025	57.3%
4	Vietnam	929	1658	56.0%	4	New Zealand	583	1020	57.2%
5	C America	810	1568	51.7%	5	Singapore	407	787	51.7%
6	Bangladesh	821	1664	49.3%	6	Sweden	626	1279	48.9%
7	Pakistan	591	1549	38.2%	7	US	804	1873	42.9%
8	Peru	520	1443	36.0%	8	Hong Kong	422	1059	39.8%
9	Morocco	234	659	35.5%	9	UK	564	1705	33.1%
10	Jordan	301	870	34.6%	10	Finland	405	1280	31.6%
11	Colombia	528	1571	33.6%	11	Germany	480	1784	26.9%
12	India	713	2239	31.8%	12	Uruguay	437	1811	24.1%
13	Dominican Rep	346	1409	24.6%	13	Canada	372	1597	23.3%
14	Venezuela	261	1186	22.0%	14	Australia	294	1263	23.3%
15	China	446	2036	21.9%	15	Austria	308	1416	21.8%
16	Thailand	249	1209	20.6%	16	Japan	208	1034	20.1%
17	Puerto Rico	374	1841	20.3%	17	Switzerland	228	1196	19.1%
18	Mexico	283	1488	19.0%	18	Korea	313	1710	18.3%
19	Brazil	255	1566	16.3%	19	Belgium	218	1286	17.0%
20	Ecuador	206	1431	14.4%	20	Turkey	256	1552	16.5%

Table 6: Baseline regression of the launch study (Cox Model)

	Patent lag five years	Patent lag ten years		
VARIABLES	(1)	(2)	(3)	(4)
Patentability (lag 10)	-0.010	0.101***	0.100***	0.015
	(0.027)	(0.031)	(0.031)	(0.036)
Innovative			0.156***	0.082***
			(0.016)	(0.021)
Innovative*patent				0.144***
				(0.029)
Log(population)	-1.120***	-1.038***	-1.052***	-1.044***
	(0.131)	(0.132)	(0.132)	(0.132)
Log(GDP per capita)	0.280***	0.264***	0.259***	0.260***
	(0.034)	(0.034)	(0.034)	(0.034)
Log(Gini)	-0.141	-0.130	-0.120	-0.127
	(0.146)	(0.145)	(0.145)	(0.145)
Log(DALY)	-0.024***	-0.024***	-0.018***	-0.018***
	(0.007)	(0.007)	(0.007)	(0.007)
Life Expectancy	0.020**	0.018**	0.018**	0.020**
	(0.008)	(0.008)	(0.008)	(0.008)
Health Expenditure/GDP	0.020	0.023*	0.024*	0.023*
	(0.013)	(0.013)	(0.013)	(0.013)
Observations	356,427	356,427	356,427	356,427
Market FE	Y	Y	Y	Y
ATC1 FE	Y	Y	Y	Y
Year FE	Y	Y	Y	Y

Notes: standard errors clustered on molecule-market in parentheses.

Table 7: Cox model of the launch study by disease category

	(1)	(2)	(3)	(4)
VARIABLES	non-communicable	infectious	HIV, Malaria, TB	Neoplasm
Patentability (lag 10)	0.073*	-0.299***	1.184***	0.119
	(0.038)	(0.102)	(0.342)	(0.093)
Innovative	0.004	0.421***	1.615***	-0.062
	(0.023)	(0.061)	(0.311)	(0.063)
Innovative*patent	0.094***	0.428***	-1.070***	-0.076
	(0.031)	(0.081)	(0.332)	(0.082)
Log(population)	-0.867***	-2.243***	-3.230***	-0.335
	(0.143)	(0.355)	(0.850)	(0.352)
Log(GDP per capita)	0.256***	0.206**	0.666***	0.256***
	(0.037)	(0.088)	(0.169)	(0.080)
Log(Gini)	-0.105	-0.176	-0.085	-0.626*
	(0.157)	(0.380)	(0.798)	(0.330)
Log(DALY)	-0.042***	0.014	0.078**	-0.421
	(0.015)	(0.009)	(0.034)	(0.411)
Life Expectancy	0.021**	0.015	0.102**	0.012
	(0.009)	(0.021)	(0.040)	(0.022)
Health Expenditure /GDP	0.024*	0.050	0.260***	-0.013
	(0.014)	(0.034)	(0.072)	(0.027)
Observations	283,961	72,466	19,893	66,013
Market FE	Y	Y	Y	Y
ATC1 FE	Y	Y	Y	Y
Year FE	Y	Y	Y	Y

Notes: Standard errors clustered on molecule-market in parentheses.

Table 8: Cox model of the launch study by income level

	(1)	(2)	(3)	(4)	(5)
Variables	High income	Middle income	Low income	Middle income Excl. China	Low income excl. India
Patentability (lag 10)	0.260***	0.025	0.128	0.049	-0.081
	(0.071)	(0.047)	(0.134)	(0.048)	(0.156)
innovative	0.320***	0.076***	-0.108	0.080***	-0.131*
	(0.053)	(0.025)	(0.067)	(0.026)	(0.079)
Innovative * patent	-0.041	0.119***	-0.168	0.131***	-0.111
	(0.059)	(0.042)	(0.109)	(0.042)	(0.120)
Log(population)	-0.096	-0.848***	-2.449**	-0.697***	-2.153**
	(0.510)	(0.165)	(1.017)	(0.165)	(1.061)
Log(GDP per capita)	0.024	0.417***	0.405**	0.525***	0.390**
	(0.112)	(0.045)	(0.191)	(0.048)	(0.195)
Log(Gini)	-0.602	-0.282*	1.740*	-0.242	1.594*
	(0.410)	(0.171)	(0.913)	(0.171)	(0.908)
Log(DALY)	-0.066***	0.008	0.043	0.007	0.048*
	(0.011)	(0.010)	(0.027)	(0.010)	(0.029)
Life Expectancy	-0.056	0.010	0.167***	0.007	0.127***
	(0.038)	(0.009)	(0.035)	(0.009)	(0.037)
Health expenditure/GDP	0.034	-0.013	-0.125	-0.012	-0.031
	(0.027)	(0.016)	(0.080)	(0.016)	(0.118)
Observations	89,837	224,692	41,898	219,007	35,832
Market FE	Y	Y	Y	Y	Y
ATC1 FE	Y	Y	Y	Y	Y
Year FE	Y	Y	Y	Y	Y

Notes: Standard errors clustered on molecule-market in parentheses. We use the income classification from the World Bank in 2000.

Table 9: Regressions on originator prices with protection expiry variables

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
VARIABLES	all molecules	By innovativeness		NCD vs. infections		HIV, Malaria, and TB	neoplasms
		innovative	additional	Non communicable	infectious		
expiry	-0.106***	-0.109***	-0.098***	-0.080***	-0.216***	-0.145	0.059
	(0.019)	(0.023)	(0.031)	(0.020)	(0.049)	(0.095)	(0.045)
Log(brands)_m	-0.022***	-0.038***	0.000	-0.020***	-0.010	-0.020	-0.016
	(0.006)	(0.009)	(0.007)	(0.006)	(0.014)	(0.024)	(0.012)
Log(brands)_m*expiry	-0.101***	-0.073***	-0.123***	-0.101***	-0.113***	-0.139**	-0.074***
	(0.008)	(0.011)	(0.010)	(0.008)	(0.019)	(0.064)	(0.019)
Log(brands)_atc4	-0.062***	-0.028***	-0.104***	-0.071***	-0.026*	-0.056**	-0.002
	(0.006)	(0.008)	(0.009)	(0.007)	(0.014)	(0.024)	(0.014)
Log(brands)_act4*expiry	0.036***	0.027***	0.041***	0.030***	0.070***	0.056	-0.037**
	(0.008)	(0.010)	(0.012)	(0.008)	(0.019)	(0.040)	(0.018)
Log(population)	0.223***	0.181***	0.262***	0.144***	0.120***	0.040***	0.136***
	(0.006)	(0.007)	(0.014)	(0.009)	(0.009)	(0.010)	(0.023)
Log(GDP per capita)	0.024***	0.038***	0.003	0.023***	0.069***	0.127**	0.003
	(0.006)	(0.009)	(0.008)	(0.006)	(0.022)	(0.051)	(0.012)
Log(Gini)	0.015	-0.091***	0.136***	0.070***	-0.018	-0.171**	-0.266***
	(0.017)	(0.024)	(0.025)	(0.019)	(0.048)	(0.086)	(0.049)
Log(DALY)	-0.137***	-0.122***	-0.142***	-0.042***	-0.112***	-0.067***	-0.093***
	(0.006)	(0.006)	(0.013)	(0.009)	(0.007)	(0.008)	(0.020)
Life Expectancy	-0.008***	-0.001	-0.012***	-0.009***	0.005*	0.032***	0.002
	(0.001)	(0.001)	(0.001)	(0.001)	(0.003)	(0.004)	(0.002)
Health expenditure/GDP	0.093***	0.076***	0.109***	0.096***	0.068***	0.072***	0.063***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.004)	(0.006)	(0.003)
retail	0.079***	0.083***	0.087***	0.073***	0.139***	0.276***	0.021
	(0.007)	(0.010)	(0.008)	(0.007)	(0.016)	(0.027)	(0.015)
Observations	95,515	51,746	43,769	78,467	17,048	6,381	15,489
Adjusted R-squared	0.968	0.972	0.961	0.970	0.930	0.862	0.966
FE	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist

Notes: Standard errors clustered on molecule-year in parentheses.

Table 10: Regressions on originator prices without protection expiry variable (Sample restricted to observations with expiry variable)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	all	By innovativeness		NCD vs. infections		HIV, Malaria,	neoplasms
VARIABLES	molecules	innovative	additional	Non-communicable	infectious	and TB	
Log(brands)_m	-0.092***	-0.087***	-0.090***	-0.091***	-0.081***	-0.069***	-0.067***
	(0.005)	(0.007)	(0.006)	(0.005)	(0.011)	(0.022)	(0.013)
Log(brands)_atc4	-0.043***	-0.016**	-0.079***	-0.055***	0.012	-0.033*	-0.007
	(0.007)	(0.008)	(0.010)	(0.007)	(0.013)	(0.017)	(0.015)
Log(population)	0.225***	0.182***	0.266***	0.148***	0.121***	0.044***	0.142***
	(0.006)	(0.007)	(0.014)	(0.009)	(0.009)	(0.011)	(0.023)
Log(GDP per capita)	0.027***	0.040***	0.009	0.027***	0.070***	0.130**	0.006
	(0.006)	(0.010)	(0.008)	(0.006)	(0.022)	(0.052)	(0.012)
Log(Gini)	-0.005	-0.106***	0.111***	0.047**	-0.031	-0.178**	-0.283***
	(0.017)	(0.023)	(0.025)	(0.019)	(0.049)	(0.089)	(0.048)
Log(DALY)	-0.139***	-0.123***	-0.144***	-0.045***	-0.113***	-0.070***	-0.099***
	(0.006)	(0.006)	(0.013)	(0.009)	(0.007)	(0.008)	(0.020)
Life Expectancy	-0.009***	-0.002	-0.014***	-0.010***	0.004	0.032***	0.001
	(0.001)	(0.001)	(0.001)	(0.001)	(0.003)	(0.005)	(0.002)
Health expenditure/GDP	0.094***	0.078***	0.110***	0.097***	0.070***	0.072***	0.064***
	(0.002)	(0.002)	(0.002)	(0.002)	(0.004)	(0.006)	(0.003)
retail	0.081***	0.082***	0.093***	0.076***	0.139***	0.283***	0.019
	(0.006)	(0.010)	(0.008)	(0.007)	(0.016)	(0.027)	(0.015)
Observations	95,515	51,746	43,769	78,467	17,048	6,381	15,489
Adjusted R-squared	0.967	0.972	0.961	0.970	0.930	0.862	0.966
FE	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist

Notes: Standard errors clustered on molecule-year in parentheses.

Table 11: Regressions on originator prices using all available observations

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	all	By innovativeness		NCD vs. infections		HIV,	neoplasms
VARIABLES	molecules	innovative	additional	Non-communicable	infectious	Malaria, and TB	
Log(brands)_m	-0.082***	-0.070***	-0.080***	-0.078***	-0.110***	-0.093***	-0.090***
	(0.005)	(0.007)	(0.007)	(0.006)	(0.013)	(0.028)	(0.010)
Log(brands)_atc4	-0.041***	-0.025***	-0.076***	-0.046***	-0.003	0.004	-0.014
	(0.007)	(0.008)	(0.011)	(0.007)	(0.017)	(0.020)	(0.011)
Log(population)	0.197***	0.164***	0.237***	0.159***	0.109***	0.006	0.143***
	(0.006)	(0.006)	(0.009)	(0.007)	(0.008)	(0.010)	(0.015)
Log(GDP per capita)	0.110***	0.102***	0.121***	0.107***	0.126***	0.141***	0.066***
	(0.003)	(0.005)	(0.005)	(0.003)	(0.012)	(0.035)	(0.007)
Standardized coef. of log(GDP per capita)	*0.026*	*0.023*	*0.030*	*0.024*	*0.044*	*0.093*	*0.020*
Log(Gini)	0.587***	0.367***	0.837***	0.652***	0.252***	-0.163**	0.030
	(0.017)	(0.023)	(0.026)	(0.019)	(0.039)	(0.067)	(0.027)
Log(DALY)	-0.143***	-0.128***	-0.160***	-0.097***	-0.110***	-0.043***	-0.105***
	(0.006)	(0.006)	(0.008)	(0.007)	(0.006)	(0.006)	(0.014)
Life Expectancy	-0.004***	-0.000	-0.006***	-0.003***	-0.003	0.034***	0.001
	(0.001)	(0.001)	(0.001)	(0.001)	(0.002)	(0.004)	(0.001)
Health expenditure/GDP	0.060***	0.054***	0.067***	0.060***	0.058***	0.068***	0.048***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.003)	(0.005)	(0.002)
retail	0.101***	0.068***	0.138***	0.101***	0.136***	0.169***	-0.004
	(0.005)	(0.008)	(0.006)	(0.005)	(0.017)	(0.022)	(0.011)
Observations	186,837	99,086	87,751	160,125	26,712	7,888	33,197
Adjusted R-squared	0.979	0.980	0.977	0.981	0.950	0.830	0.968
FE	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist

Notes: Standard errors clustered on molecule-year in parentheses. Standardized coefficients are calculated as coefficient*s.d.(x)/s.d.(y) where standard errors are based on the corresponding subsample used in each regression.

Table 12: Regressions on generic prices using all available observations

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
VARIABLES		By innovativeness		NCD vs. infections		HIV,	neoplasms
	all molecules	innovative	additional	Non-communicable	infectious	Malaria, and TB	
Log(brands)_m	-0.147***	-0.134***	-0.137***	-0.145***	-0.152***	-0.170***	-0.068**
	(0.009)	(0.013)	(0.011)	(0.010)	(0.019)	(0.045)	(0.034)
Log(brands)_atc4	0.006	0.034**	-0.052***	-0.014	0.151***	0.320***	0.055*
	(0.009)	(0.014)	(0.011)	(0.010)	(0.023)	(0.041)	(0.033)
Log(population)	0.225***	0.257***	0.150***	0.168***	0.189***	0.171***	0.229***
	(0.010)	(0.013)	(0.013)	(0.012)	(0.017)	(0.023)	(0.032)
Log(GDP per capita)	0.259***	0.316***	0.203***	0.248***	0.343***	0.686***	0.317***
	(0.006)	(0.009)	(0.007)	(0.006)	(0.018)	(0.048)	(0.017)
Standardized coef. of log(GDP per capita)	*0.084*	*0.083*	*0.090*	*0.078*	*0.203*	*0.498*	*0.119*
Log(Gini)	1.066***	0.635***	1.487***	1.197***	0.173***	-1.014***	0.218***
	(0.025)	(0.036)	(0.029)	(0.026)	(0.066)	(0.204)	(0.065)
Log(DALY)	-0.207***	-0.233***	-0.131***	-0.142***	-0.224***	-0.153***	-0.187***
	(0.010)	(0.014)	(0.013)	(0.012)	(0.017)	(0.023)	(0.032)
Life Expectancy	0.005***	-0.002	0.014***	0.010***	-0.022***	-0.008	0.001
	(0.001)	(0.002)	(0.001)	(0.001)	(0.004)	(0.008)	(0.003)
Health expenditure/GDP	0.002	0.007***	-0.004	-0.002	0.021***	0.010	-0.007*
	(0.002)	(0.003)	(0.003)	(0.002)	(0.006)	(0.015)	(0.004)
retail	0.188***	0.188***	0.194***	0.184***	0.293***	0.787***	0.208***
	(0.008)	(0.012)	(0.012)	(0.009)	(0.026)	(0.075)	(0.026)
Observations	89,740	42,534	47,206	78,830	10,910	1,521	12,434
Adjusted R-squared	0.944	0.961	0.905	0.948	0.806	0.714	0.901
FE	Year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist

Notes: Standard errors clustered on molecule-year in parentheses. Standardized coefficients are calculated as coefficient*s.d.(x)/s.d.(y) where standard errors are based on the corresponding subsample used in each regression.

Table 13: Regressions on originator prices using all available observations
Robustness check using brands count by ATC3

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	all	By innovativeness		NCD vs. infections		HIV, Malaria,	neoplasms
VARIABLES	molecules	innovative	additional	Non-communicable	infectious	and TB	
Log(brands)_m	-0.093***	-0.074***	-0.096***	-0.091***	-0.109***	-0.071***	-0.100***
	(0.005)	(0.006)	(0.006)	(0.005)	(0.012)	(0.027)	(0.010)
Log(brands)_atc3	-0.025***	-0.022***	-0.050***	-0.027***	-0.006	-0.030	0.004
	(0.006)	(0.008)	(0.009)	(0.006)	(0.017)	(0.019)	(0.011)
Log(population)	0.196***	0.164***	0.237***	0.159***	0.109***	0.006	0.143***
	(0.006)	(0.006)	(0.009)	(0.007)	(0.009)	(0.010)	(0.015)
Log(GDP per capita)	0.110***	0.102***	0.120***	0.106***	0.126***	0.148***	0.064***
	(0.003)	(0.005)	(0.005)	(0.003)	(0.012)	(0.036)	(0.008)
Log(Gini)	0.589***	0.367***	0.839***	0.653***	0.252***	-0.181***	0.033
	(0.017)	(0.023)	(0.026)	(0.019)	(0.038)	(0.067)	(0.027)
Log(DALY)	-0.144***	-0.128***	-0.163***	-0.099***	-0.110***	-0.040***	-0.108***
	(0.006)	(0.006)	(0.008)	(0.007)	(0.006)	(0.006)	(0.014)
Life Expectancy	-0.004***	-0.000	-0.007***	-0.003***	-0.003	0.033***	0.001
	(0.001)	(0.001)	(0.001)	(0.001)	(0.002)	(0.004)	(0.001)
Health expenditure/GDP	0.060***	0.054***	0.067***	0.060***	0.058***	0.070***	0.048***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.003)	(0.005)	(0.002)
retail	0.101***	0.068***	0.137***	0.101***	0.136***	0.165***	-0.001
	(0.005)	(0.008)	(0.006)	(0.005)	(0.017)	(0.022)	(0.011)
Observations	186,837	99,086	87,751	160,125	26,712	7,888	33,197
Adjusted R-squared	0.979	0.980	0.977	0.981	0.950	0.830	0.968
FE	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist

Notes: Standard errors clustered on molecule-year in parentheses.

Table 14: Regressions on generic prices using all available observations
Robustness check using brands count by ATC3

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
VARIABLES		By innovativeness		NCD vs. infections		HIV, Malaria, and TB	neoplasms
	all molecules	innovative	additional	Non-communicable	infectious		
Log(brands)_m	-0.137***	-0.115***	-0.136***	-0.132***	-0.159***	-0.133***	-0.020
	(0.008)	(0.012)	(0.011)	(0.009)	(0.018)	(0.034)	(0.037)
Log(brands)_atc3	-0.013	0.005	-0.060***	-0.040***	0.181***	0.314***	-0.018
	(0.009)	(0.015)	(0.011)	(0.010)	(0.023)	(0.047)	(0.045)
Log(population)	0.226***	0.258***	0.152***	0.170***	0.183***	0.179***	0.225***
	(0.010)	(0.013)	(0.013)	(0.012)	(0.017)	(0.024)	(0.033)
Log(GDP per capita)	0.259***	0.316***	0.204***	0.248***	0.346***	0.676***	0.321***
	(0.006)	(0.009)	(0.007)	(0.006)	(0.018)	(0.046)	(0.018)
Log(Gini)	1.066***	0.634***	1.486***	1.194***	0.155**	-0.964***	0.216***
	(0.025)	(0.036)	(0.029)	(0.026)	(0.066)	(0.211)	(0.065)
Log(DALY)	-0.205***	-0.230***	-0.131***	-0.140***	-0.226***	-0.161***	-0.175***
	(0.010)	(0.014)	(0.013)	(0.012)	(0.017)	(0.023)	(0.034)
Life Expectancy	0.006***	-0.001	0.014***	0.011***	-0.023***	-0.010	0.001
	(0.001)	(0.002)	(0.001)	(0.001)	(0.004)	(0.008)	(0.003)
Health expenditure/GDP	0.002	0.008***	-0.004	-0.002	0.021***	0.008	-0.007
	(0.002)	(0.003)	(0.003)	(0.002)	(0.006)	(0.015)	(0.004)
retail	0.187***	0.185***	0.193***	0.183***	0.301***	0.810***	0.197***
	(0.009)	(0.013)	(0.012)	(0.009)	(0.026)	(0.069)	(0.028)
Observations	89,740	42,534	47,206	78,830	10,910	1,521	12,434
Adjusted R-squared	0.944	0.961	0.905	0.948	0.806	0.713	0.901
FE	Year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist	year_mlist

Notes: Standard errors clustered on molecule-year in parentheses.

Table 15: Robustness analyses of the launch study

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Baseline Cox	Parametric model		Market*ATC1 Fixed Effects			
VARIABLES		Gompertz	Weibull	Full sample	High	Middle	Low
Patentability	0.015	0.007	0.514***	0.041	0.238***	0.072	0.136
	(0.036)	(0.035)	(0.036)	(0.036)	(0.073)	(0.047)	(0.132)
Innovative	0.082***	0.092***	0.184***	0.094***	0.301***	0.087***	-0.098
	(0.021)	(0.021)	(0.023)	(0.021)	(0.055)	(0.025)	(0.066)
Innovative*patent	0.144***	0.141***	0.147***	0.104***	-0.027	0.072*	-0.224**
	(0.029)	(0.029)	(0.031)	(0.030)	(0.061)	(0.043)	(0.112)
Log(population)	-1.044***	-0.993***	-0.592***	-0.773***	0.069	-0.657***	-2.828***
	(0.132)	(0.133)	(0.128)	(0.134)	(0.516)	(0.168)	(1.022)
Log(GDP per capita)	0.260***	0.248***	0.249***	0.272***	0.050	0.415***	0.305
	(0.034)	(0.034)	(0.033)	(0.035)	(0.112)	(0.046)	(0.190)
Log(Gini)	-0.127	-0.101	-0.156	-0.125	-0.696*	-0.318*	1.820**
	(0.145)	(0.145)	(0.140)	(0.145)	(0.418)	(0.170)	(0.905)
Log(DALY)	-0.018***	-0.018***	-0.010	-0.043***	-0.077***	-0.019*	0.048
	(0.007)	(0.007)	(0.007)	(0.008)	(0.012)	(0.011)	(0.032)
Life Expectancy	0.020**	0.019**	0.016**	0.023***	-0.089**	0.011	0.187***
	(0.008)	(0.008)	(0.008)	(0.008)	(0.039)	(0.009)	(0.036)
Health Expenditure/GDP	0.023*	0.020	0.013	0.025*	0.048*	-0.012	-0.136*
	(0.013)	(0.013)	(0.012)	(0.013)	(0.028)	(0.016)	(0.081)
Observations	356,427	356,427	356,427	356,427	89,837	224,692	41,898
Market FE, ATC1 FE	Y	Y	Y	-	-	-	-
Year FE	Y	Y	Y	Y	Y	Y	Y
Market*ATC1 FE	N	N	N	Y	Y	Y	Y

Notes: Standard errors clustered on molecule-market in parentheses. We conduct Market*ATC1 fixed effects by stratification.

Table 16: Launch regressions with interaction terms of innovativeness

	(1)	(2)	(3)	(4)	(5)	(6)
	Baseline Cox	Interaction terms	With interaction terms by income			Gompertz
VARIABLES			High	Middle	Low	
Patentability	0.015	0.099***	0.303***	0.043	0.203	0.099***
	(0.036)	(0.037)	(0.075)	(0.049)	(0.153)	(0.037)
Innovative	0.082***	0.655	2.276	1.127**	-1.442	0.795*
	(0.021)	(0.427)	(1.385)	(0.554)	(2.831)	(0.423)
Innovative*patent	0.144***	0.008	-0.099	0.092**	-0.291	-0.008
	(0.029)	(0.035)	(0.071)	(0.047)	(0.181)	(0.035)
Log(population)	-1.044***	-1.004***	-0.059	-0.828***	-2.587**	-0.953***
	(0.132)	(0.133)	(0.510)	(0.167)	(1.014)	(0.133)
Log(GDP per capita)	0.260***	0.228***	0.059	0.388***	0.508**	0.208***
	(0.034)	(0.036)	(0.120)	(0.048)	(0.198)	(0.036)
Log(Gini)	-0.127	-0.082	-0.224	-0.247	1.560*	-0.046
	(0.145)	(0.149)	(0.436)	(0.176)	(0.944)	(0.149)
Log(DALY)	-0.018***	0.013	0.004	0.019	-0.034	0.013
	(0.007)	(0.011)	(0.018)	(0.015)	(0.048)	(0.011)
Life Expectancy	0.020**	0.022**	-0.053	0.016	0.171***	0.021**
	(0.008)	(0.009)	(0.039)	(0.010)	(0.036)	(0.009)
Health Expenditure/GDP	0.023*	0.009	0.026	-0.009	-0.185**	0.009
	(0.013)	(0.013)	(0.029)	(0.017)	(0.087)	(0.013)
lnpop_invt		0.044***	0.155***	-0.001	-0.120	0.049***
		(0.015)	(0.029)	(0.022)	(0.081)	(0.015)
lnpcgdp_invt		0.085***	-0.043	0.054	-0.263**	0.101***
		(0.024)	(0.073)	(0.034)	(0.106)	(0.023)
lngini_invt		-0.093	-0.636***	-0.080	0.361	-0.111
		(0.072)	(0.239)	(0.087)	(0.694)	(0.071)
lndaly_invt		-0.037***	-0.084***	-0.014	0.098*	-0.038***
		(0.011)	(0.016)	(0.015)	(0.052)	(0.011)
Life expectancy_invt		-0.006	0.004	-0.010*	-0.008	-0.007
		(0.004)	(0.016)	(0.006)	(0.010)	(0.004)
Hlth/gdp_invt		0.023**	0.013	-0.006	0.111	0.019**
		(0.009)	(0.018)	(0.013)	(0.069)	(0.009)
Observations	356,427	356,427	89,837	224,692	41,898	356,427
Market FE	Y	Y	Y	Y	Y	Y
ATC FE	Y	Y	Y	Y	Y	Y
Year FE	Y	Y	Y	Y	Y	Y

Notes: Standard errors clustered on molecule-market in parentheses. Results from column (1) to column (5) are estimated by Cox model. Column (6) is estimated by parametric proportional hazard model with Gompertz distribution.

APPENDIX

Table A1a: the number of molecule-market combinations by launch outcome and by income level (556 molecules in 70 markets)

Launch Outcome	Low Income		Middle Income		High Income		Total
	No Patent	Patent	No Patent	Patent	No Patent	Patent	
# No launch	888	726	5,807	2,492	1,037	2,858	13,808
# Launch	1,118	604	8,231	4,598	2,055	8,506	25,112
Total	2,006	1,330	14,038	7,090	3,092	11,364	**38,920**

Notes: Among 25112 launched molecule-market combinations, 382 launch records have no specified launch date. Income level is based on classification in 2000 by the World Bank.

Table A1b: the number of local launches by firm type

Launch outcome	If the launch date is specified	First launches by firm type
Total Launches (25112)	Specified date: 24730 Unspecified date: 382	Originators/licensees: 22778 Generic firms: 2334

Table A2: Summary of pharmaceutical sample and market sample we use

	Total	By innovativeness		No. of markets	Reasons of restriction to a smaller set
		innovative	Non-innovative (additional)		
All molecules	578	307	271	70	N/A
Panel A: Launch Study					
Summary statistics (incl. survival estimates)	556	294	262	70	We drop 22 molecules whose global launch took place before 1980. Since all medicines were approved by USFAD from 1987 to 2011, those early launches may be other versions of the molecule.
Cox model	540	293	247	63	Among the 556 molecules, 16 are dropped in regressions due to no data on disease burden to link.
Panel B: Price Study					
summary statistics: Originator prices	573	305	268	70	Originator products of five molecules were discontinued or withdrawn before 2007 in our sample markets.
summary statistics: generic prices	504	254	250	70	Given 578 molecules, only 504 molecules have generic versions on any of the markets in our sample.
Coverage of IQVIA protection data	465	236	229	59	We matched protection data of 481 molecules in 59 markets. 16 molecules are dropped due to no DALY to link. Noticeably, protection data set is highly unbalanced. Composition of molecules whose protection data is available varies by market.
OLS regression: Originator prices	557	304	253	63	Among the 573 molecules, 16 molecules are dropped in regression due to no disease burden to link. Seven markets are not present in regressions due to missing Gini.
OLS regression: Generics prices	489	253	236	63	Among the 504 molecules, 15 molecules are dropped in regression due to no disease burden to link. Seven markets are not present in regressions due to missing Gini.

Table A3: Summary of markets in this study

No.	Market	income level in 2000	IQVIA data source	IQVIA protection data availability	market dropped in regressions due to missing variable
1	Algeria	LM	retail only	1	
2	Argentina	UM	retail only	1	
3	Australia	H	combined	1	
4	Austria	H	combined	1	
5	Bangladesh	L	retail only	0	
6	Belgium	H	combined	1	
7	Brazil	UM	retail only	1	
8	Bulgaria	LM	combined	1	
9	C America	LM	retail only	0	
10	Canada	H	combined	1	
11	Chile	UM	retail only	1	
12	China	LM	hospital only	1	
13	Colombia	LM	retail only	1	
14	Croatia	UM	combined	1	
15	Czech	UM	combined	1	
16	Dominican Rep	LM	retail only	0	
17	Ecuador	LM	retail only	1	
18	Egypt	LM	retail only	1	
19	Estonia	UM	retail only	1	
20	Finland	H	combined	1	
21	Fr W Africa	L	retail only	0	
22	France	H	combined	1	
23	Germany	H	combined	1	
24	Greece	H	retail only	1	
25	Hong Kong	H	combined	0	no Gini, no DALY
26	Hungary	UM	combined	1	
27	India	L	combined	1	
28	Indonesia	L	combined	1	
29	Ireland	H	combined	1	
30	Italy	H	combined	1	
31	Japan	H	combined	1	
32	Jordan	LM	retail only	0	
33	Kazakhstan	LM	retail -> combined [a]	0	
34	Korea	UM	combined	1	
35	Kuwait	H	retail only	0	no Gini
36	Latvia	LM	retail only	1	
37	Lebanon	UM	retail only	0	
38	Lithuania	LM	combined	1	
39	Luxembourg	H	retail only	0	
40	Malaysia	UM	combined	1	
41	Mexico	UM	retail only	1	

No.	Market	income level in 2000	IQVIA data source	IQVIA protection data availability	market dropped in regressions due to missing variable
42	Morocco	LM	retail only	1	
43	Netherlands	H	retail only	1	
44	New Zealand	H	combined	1	no Gini
45	Norway	H	combined	1	
46	Pakistan	L	retail only	1	
47	Peru	LM	retail only	1	
48	Philippines	LM	combined	1	
49	Poland	UM	combined	1	
50	Portugal	H	retail -> combined [b]	1	
51	Puerto Rico	UM	combined	1	no Gini; no DALY
52	Romania	LM	combined	1	
53	Russia	LM	combined	1	
54	Saudi Arabia	UM	retail -> combined [c]	1	no Gini
55	Singapore	H	combined	0	no Gini
56	Slovakia	UM	combined	1	
57	Slovenia	H	combined	1	
58	South Africa	UM	combined	1	
59	Spain	H	combined	1	
60	Sweden	H	combined	1	
61	Switzerland	H	combined	1	
62	Thailand	LM	combined	1	
63	Tunisia	LM	retail only	1	
64	Turkey	UM	combined	1	
65	UAE	H	retail only	1	no Gini
66	UK	H	combined	1	
67	US	H	combined	1	
68	Uruguay	UM	combined	1	
69	Venezuela	UM	retail only	1	
70	Vietnam	L	combined	1	

Notes:

a: In Kazakhstan, given data availability from 2007 to 2017, data from retail channel is available since 2007, but hospital data is available since 2008.

b: In Portugal, given data availability from 2007 to 2017, data from retail channel is available since 2007, but hospital data is available since 2010.

c: In Saudi Arabia, given data availability from 2007 to 2017, data from retail channel is available since 2007, but tender data is available since 2014.

———